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(54) Title: EPOTHILONE MINOR CONSTITUENTS			
(54) Bezeichnung: EPOTHILON-NEBENKOMPONENTEN			
(57) Abstract			
The invention relates to compounds which are obtained by fermenting DSM 6773, especially epothilones A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 and K and trans-epothilones C1 and C2.			
(57) Zusammenfassung			
Die Erfindung betrifft Verbindungen, die durch Fermentation von DSM 6773 erhältlich sind, insbesondere Epothilone A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 und K und Trans-Epothilone C1 und C2.			

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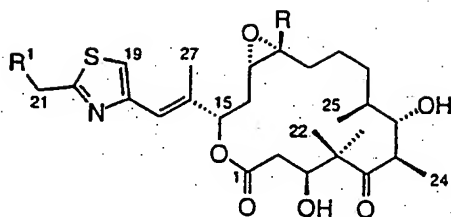
Epothilon-Nebenkomponenten

Die Erfindung betrifft Verbindungen, die im vorliegenden Zusammenhang als Epothilon-Nebenkomponenten bezeichnet werden, und zwar Verbindungen 5 bis 13 und 16 bis 39. Diese Verbindungen lassen sich durch Fermentation von DSM 6773 gemäß DE 41 38 042.8 gewinnen.

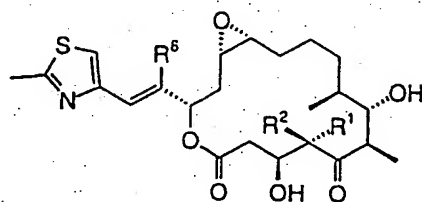
Kenndaten der erfindungsgemäßen Verbindungen sind im folgenden zusammengestellt.

Gewinnung: Die Aufarbeitung eines Rohepothilon-Gemischs, das durch Fermentation von DSM 6773 in einem 900 Liter-Fermentator gewonnen wurde, ist schematisch Fig. 1 bis 2 zu entnehmen.

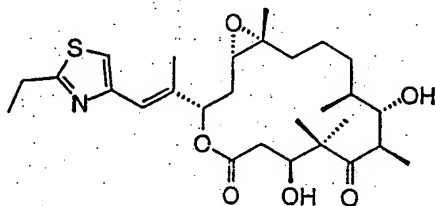
Aktivitäten: vgl. Tab. 1



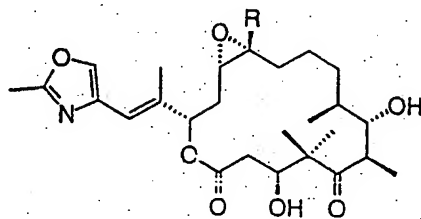
- Epothilone A (1) $R^1 = H$; $R = H$
 Epothilone B (2) $R^1 = H$; $R = Me$
 Epothilone E (3) $R^1 = OH$; $R = H$
 Epothilone F (4) $R^1 = OH$; $R = Me$



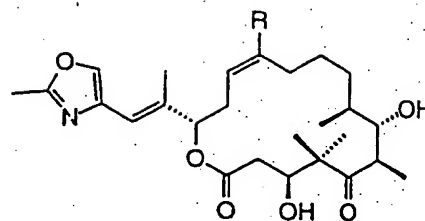
- Epothilone A₁ (5) $R^1 = H$; $R^2, R^8 = Me$
 Epothilone A₂ (6) $R^2 = H$; $R^1, R^8 = Me$
 Epothilone A₈ (7) $R^8 = H$; $R^1, R^2 = Me$
 Epothilone A₉ (8) $R^1 = CH_2OH$; $R^2, R^8 = Me$



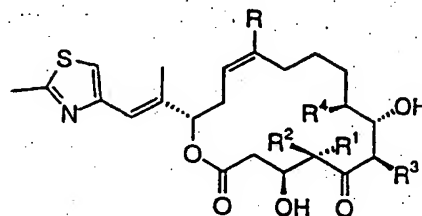
Epothilone B₁₀ (9)



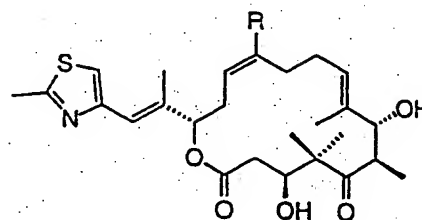
- Epothilone G₁ (10) $R = H$
 Epothilone G₂ (11) $R = Me$



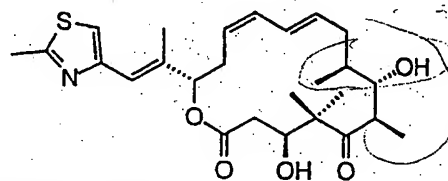
- Epothilone H₁ (12) $R = H$
 Epothilone H₂ (13) $R = Me$



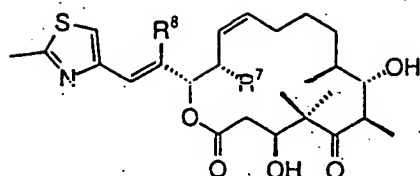
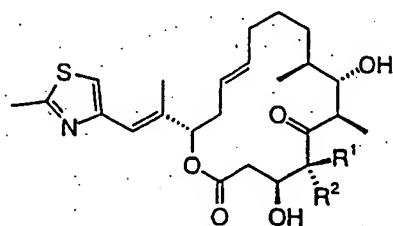
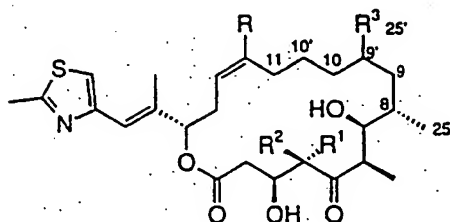
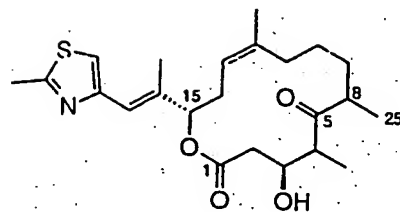
- Epothilone C (14) $R^1, R^2, R^3, R^4 = Me$; $R = H$
 Epothilone D (15) $R^1, R^2, R^3, R^4, R = Me$
 Epothilone C₁ (16) $R^1 = H$; $R^2, R^3, R^4 = Me$; $R = H$
 Epothilone D₁ (17) $R^1 = H$; $R^2, R^3, R^4 = Me$; $R = Me$
 Epothilone C₂ (18) $R^2 = H$; $R^1, R^3, R^4 = Me$; $R = H$
 Epothilone D₂ (19) $R^2 = H$; $R^1, R^3, R^4 = Me$; $R = Me$
 Epothilone C₃ (20) $R^3 = H$; $R^1, R^2, R^4 = Me$; $R = H$
 Epothilone C₄ (21) $R^4 = H$; $R^1, R^2, R^3 = Me$; $R = H$



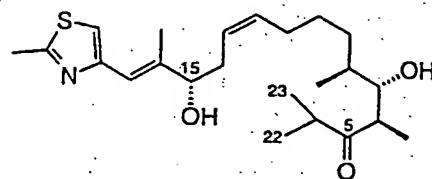
- Epothilone C₅ (22) $R = H$
 Epothilone D₅ (23) $R = Me$



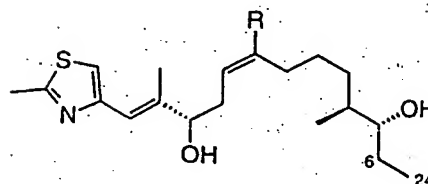
Epothilone C₆ (24)

Epothilone C₇ (25) R⁷ = OH; R⁸ = MeEpothilone C₈ (26) R⁸, R⁷ = HEpothilone C₉ (27) R⁸ = CH₂OH; R⁷ = Htrans-Epothilone C₁ (28) R¹ = H; R² = Metrans-Epothilone C₂ (29) R² = H; R¹ = MeEpothilone I₁ (30) R, R³ = H; R¹, R² = MeEpothilone I₂ (31) R = H; R¹, R², R³ = MeEpothilone I₃ (32) R¹, R², R³, R = MeEpothilone I₄ (33) R², R = H; R¹, R³ = MeEpothilone I₅ (34) R² = H; R¹, R³, R = MeEpothilone I₆ (35) R¹ = H; R², R³, R = Me

Epothilone K (36)



(37)



(38) R = H

(39) R = Me

Epothilone A₁ (5): colorless amorphous solid; $[\alpha]_D^{22}$ -69 (c 0.1, MeOH); UV (MeOH) λ_{\max} nm (ε) 208 (19600), 247 (13600); IR (KBr) ν_{\max} 3437, 2959, 2931, 2876, 1732, 1710, 1455, 1259, 978 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.95 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.68 (1H, dd, J = 4.4, 4.0 Hz, H-15), 4.12 (1H, m, H-3), 3.71 (1H, m, H-7), 3.52 (1H, bs, 7-OH), 3.37 (1H, bd, J = 7.5 Hz, 3-OH), 3.21 (1H, dq, J = 7.7, 7.0 Hz, H-4), 3.02 (1H, ddd, J = 9.2, 4.5, 2.8 Hz, H-13), 2.87 (1H, ddd, J = 8.3, 4.5, 3.7 Hz, H-12), 2.78 (1H, dd, J = 16.8, 4.3 Hz, H-2a), 2.70 (3H, s, H-21), 2.66 (1H, dq, J = 3.9, 7.0 Hz, H-6), 2.65 (1H, dd, J = 16.8, 5.2 Hz, H-2b), 2.16 (1H, ddd, J = 15.4, 4.4, 2.8 Hz, H-14a), 2.12 (3H, bs, H-27), 1.91 (1H, ddd, J = 15.4, 9.2, 4.0 Hz, H-14b), 1.63 (1H, m, H-10a), 1.62 (2H, m, H-11), 1.59 (1H, m, H-9a), 1.52 (1H, m, H-10b), 1.39 (1H, m, H-8), 1.35 (1H, m, H-9b), 1.211 (3H, d, J = 7.0 Hz, H-23), 1.207 (3H, d, J = 7.0 Hz, H-24), 0.89 (3H, d, J = 6.9 Hz, H-25); EIMS m/z 479 $[\text{M}]^+$ (21), 322 (31), 306 (65), 304 (47), 168 (45), 166 (73), 164 (100), 151 (30), 140 (35); HREIMS m/z 479.2317 (calcd. for $\text{C}_{27}\text{H}_{41}\text{NO}_5\text{S}$, 479.2342).

Epothilone A₂ (6): colorless amorphous solid; $[\alpha]_D^{22}$ +12.0 (c 1.0, MeOH); UV (MeOH) λ_{\max} nm (ε) 210 (15100), 248 (15500); IR (KBr) ν_{\max} 3438, 2963, 2929, 2875, 1734, 1706, 1458, 1262, 981 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.98 (1H, s, H-19), 6.63 (1H, bs, H-17), 5.40 (1H, dd, J = 8.3, 3.4 Hz, H-15), 4.26 (1H, ddd, J = 8.5, 4.8, 4.7 Hz, H-3), 3.85 (1H, dd, J = 7.9,

2.6 Hz, H-7), 3.54 (1H, bs, 3-OH), 3.09 (1H, dq, $J = 4.8, 7.0$ Hz, H-4), 3.01 (1H, ddd, $J = 8.3, 4.8, 4.6$ Hz, H-13), 2.98 (1H, dq, $J = 7.9, 7.0$ Hz, H-6), 2.89 (1H, ddd, $J = 6.7, 4.6, 4.4$ Hz, H-12), 2.68 (3H, s, H-21), 2.60 (1H, dd, $J = 15.1, 8.5$ Hz, H-2a), 2.52 (1H, bs, 7-OH), 2.50 (1H, dd, $J = 15.1, 4.7$ Hz, H-2b), 2.18 (1H, ddd, $J = 15.0, 4.8, 3.4$ Hz, H-14a), 2.11 (3H, d, $J = 1.3$ Hz, H-27), 1.82 (1H, ddd, $J = 15.0, 8.3, 8.1$ Hz, H-14b), 1.63 (1H, m, H-8), 1.61 (2H, m, H-11a and H-10a), 1.46 (1H, m, H-11b), 1.39 (2H, m, H-9), 1.31 (1H, m, H-10b), 1.22 (3H, d, $J = 7.0$ Hz, H-24), 1.15 (3H, d, $J = 7.0$ Hz, H-22), 1.01 (3H, d, $J = 6.9$ Hz, H-25); ^{13}C NMR (CDCl_3 , 100 MHz) δ 216.2 (s, C-5), 170.1 (s, C-1), 164.9 (s, C-20), 152.0 (s, C-18), 137.0 (s, C-16), 120.3 (d, C-17), 116.5 (d, C-19), 76.7 (d, C-15), 75.6 (d, C-7), 69.1 (d, C-3), 57.1 (d, C-12), 54.3 (d, C-13), 50.3 (d, C-4), 49.6 (d, C-6), 39.4 (t, C-2), 35.5 (d, C-8), 32.2 (t, C-14), 29.6 (t, C-9), 27.6 (t, C-11), 23.9 (t, C-10), 19.2 (q, C-21), 18.0 (q, C-25), 15.6 (q, C-27), 13.9 (q, C-24), 12.4 (q, C-22); EIMS m/z 479 $[\text{M}]^+$ (18), 322 (38), 306 (78), 304 (59), 168 (48), 166 (96), 164 (100), 151 (33), 140 (38); HREIMS m/z 479.2318 (calcd. for $\text{C}_{27}\text{H}_{41}\text{NO}_5\text{S}$, 479.2342).

Epothilone A₃ (7): colorless amorphous solid; $[\alpha]_D^{22} -76.2$ (c 1.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 210 (15300), 248 (15500); IR (KBr) ν_{max} 3440, 2967, 2932, 2876, 1736, 1691, 1467, 1252, 979 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.95 (1H, s, H-19), 6.64 (1H, dd, $J = 15.6, 0.9$ Hz, H-17), 6.52 (1H, dd, $J = 15.6, 6.6$ Hz, H-16), 5.68 (1H, dddd, $J = 7.8, 6.6, 3.2, 0.9$ Hz, H-15), 4.11 (1H, ddd, $J = 10.1, 6.6, 3.5$ Hz, H-3), 3.78 (1H, ddd, $J = 5.2, 3.2, 3.2$ Hz, H-7), 3.66 (1H, d, $J = 6.6$ Hz, 3-OH), 3.23 (1H, dq, $J = 5.2, 6.9$ Hz, H-6), 3.08 (1H, ddd, $J = 7.3, 5.5, 4.1$ Hz, H-13), 2.90 (1H, ddd, $J = 6.6, 4.6, 4.1$ Hz, H-12), 2.69 (3H, s, H-21), 2.52 (1H, dd, $J = 14.7, 10.1$ Hz, H-2a), 2.44 (1H, bd, $J = 3.2$ Hz, 7-OH), 2.41 (1H, dd, $J = 14.7, 3.5$ Hz, H-2b), 2.10

(1H, ddd, $J = 15.0, 5.5, 3.2$ Hz, H-14a), 1.90 (1H, ddd, $J = 15.0, 7.8, 7.3$ Hz, H-14b), 1.71 (1H, m, H-8), 1.65 (1H, m, H-11a), 1.50 (1H, m, H-10a), 1.47 (1H, m, H-11b), 1.40 (2H, m, H-9), 1.39 (1H, m, H-10b), 1.33 (3H, s, H-23), 1.16 (3H, d, $J = 6.9$ Hz, H-24), 1.08 (3H, s, H-22), 0.98 (3H, d, $J = 7.0$ Hz, H-25); ^{13}C NMR (CDCl_3 , 75 MHz) δ 220.3 (s, C-5), 170.7 (s, C-1), 166.5 (s, C-20), 152.2 (s, C-18), 128.4 (d, C-16), 125.9 (d, C-17), 116.4 (d, C-19), 75.0 (d, C-7), 73.6 (d, C-3), 72.7 (d, C-15), 57.3 (d, C-12), 54.1 (d, C-13), 52.6 (s, C-4), 43.8 (d, C-6), 38.9 (t, C-2), 36.3 (d, C-8), 32.5 (t, C-14), 30.3 (t, C-9), 26.7 (t, C-11), 24.0 (t, C-10), 21.3 (q, C-23), 21.0 (q, C-22), 19.3 (q, C-21), 17.1 (q, C-25), 14.5 (q, C-24); EIMS m/z 479 $[\text{M}]^+$ XXX; HRDCIMS m/z 480.2401 (calcd. for $\text{C}_{25}\text{H}_{38}\text{NO}_6\text{S}$, 480.2401).

Epothilone A₉ (8): colorless amorphous solid; $[\alpha]_D^{22} -37.6$ (c 0.5, MeOH); UV (MeOH) λ_{max} nm (ϵ) 211 (15500), 253 (14100); IR (KBr) ν_{max} 3423, 2965, 2932, 2877, 1736, 1690, 1463, 1249, 1014, 979 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.10 (1H, s, H-19), 6.72 (1H, dd, $J = 10.7, 4.3$ Hz, 27-OH), 6.60 (1H, bs, H-17), 5.69 (1H, dd, $J = 11.6, 2.0$ Hz, H-15), 5.59 (1H, d, $J = 6.6$ Hz, 3-OH), 4.49 (1H, ddd, $J = 12.9, 4.3, 1.2$ Hz, H-27a), 4.27 (1H, ddd, $J = 11.6, 6.6, 2.9$ Hz, H-3), 4.11 (1H, ddd, $J = 12.9, 10.7, 1.0$ Hz, H-27b), 3.71 (1H, ddd, $J = 4.8, 3.0, 2.8$ Hz, H-7), 3.17 (1H, dq, $J = 3.0, 6.8$ Hz, H-6), 3.04 (1H, ddd, $J = 9.7, 3.6, 2.2$ Hz, H-13), 2.93 (1H, bs, 7-OH), 2.91 (1H, ddd, $J = 9.7, 3.6, 2.7$ Hz, H-12), 2.72 (3H, s, H-21), 2.48 (1H, dd, $J = 14.2, 11.6$ Hz, H-2a), 2.11 (1H, dd, $J = 14.2, 2.9$ Hz, H-2b), 2.03 (1H, ddd, $J = 14.7, 2.2, 2.0$ Hz, H-14a), 1.86 (1H, m, H-11a), 1.85 (1H, m, H-14b), 1.79 (1H, m, H-8), 1.52 (1H, m, H-10a), 1.37 (3H, m, H-9 and H-10b), 1.37 (3H, s, H-23), 1.36 (1H, m, H-11b), 1.19 (3H, d, $J = 6.8$ Hz, H-24), 1.02 (3H, d, $J = 7.1$ Hz, H-25), 1.00 (3H, s, H-22); ^{13}C NMR (CDCl_3 , 75 MHz) δ 220.5 (s, C-5).

170.2 (s, C-1), 167.5 (s, C-20), 150.7 (s, C-18), 138.9 (s, C-16), 125.2 (d, C-17), 119.5 (d, C-19), 76.7 (d, C-15), 73.4 (d, C-7), 70.4 (d, C-3), 57.7 (d, C-12), 57.2 (t, C-27), 55.3 (d, C-13), 54.2 (s, C-4), 41.3 (d, C-6), 40.7 (t, C-2), 37.5 (d, C-8), 31.8 (t, C-14), 31.2 (t, C-9), 28.0 (t, C-11), 23.7 (q, C-23), 23.2 (t, C-10), 19.2 (q, C-21), 16.8 (q, C-22), 15.8 (q, C-25), 13.5 (q, C-24); EIMS m/z 509 $[M]^+$ (9), 491 (4), 322 (28), 321 (25), 180 (45), 167 (40), 166 (100), 165 (49), 154 (47), 138 (33); HREIMS m/z 509.2467 (calcd. for $C_{26}H_{39}NO_7S$, 509.2447).

Epothilone B₁₀ (9): colorless amorphous solid; $[\alpha]_D^{22}$ -27 (c 0.15, MeOH); UV (MeOH) λ_{max} nm (ϵ) 212 (15800), 247 (12500); IR (KBr) ν_{max} 3434, 2962, 2930, 2876, 2858, 1733, 1692, 1461, 1259, 1052, 981 cm^{-1} ; 1H NMR ($CDCl_3$, 600 MHz) δ 6.99 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.42 (1H, dd, J = 8.0, 3.0 Hz, H-15), 4.25 (1H, ddd, J = 9.5, 6.3, 2.8 Hz, H-3), 4.23 (1H, bs, 3-OH), 3.77 (1H, ddd, J = 4.0, 3.9, 3.8 Hz, H-7), 3.30 (1H, dq, J = 4.0, 6.9 Hz, H-6), 3.01 (2H, q, J = 7.6 Hz, H-21), 2.81 (1H, dd, J = 7.7, 4.6 Hz, H-13), 2.68 (1H, bs, 7-OH), 2.54 (1H, dd, J = 13.9, 9.5 Hz, H-2a), 2.36 (1H, dd, J = 13.9, 2.8 Hz, H-2b), 2.11 (1H, ddd, J = 15.3, 4.6, 3.0 Hz, H-14a), 2.09 (3H, s, H-27), 1.91 (1H, ddd, J = 15.3, 8.0, 7.7 Hz, H-14b), 1.74 (1H, m, H-8), 1.73 (1H, m, H-11a), 1.51 (1H, m, H-10a), 1.41 (1H, m, H-11b), 1.39 (3H, t, J = 7.6 Hz, H-28), 1.38 (3H, m, H-9 and H-10b), 1.37 (3H, s, H-23), 1.28 (3H, s, H-26), 1.17 (3H, d, J = 6.9 Hz, H-24), 1.09 (3H, s, H-22), 1.01 (3H, d, J = 7.0 Hz, H-25); EIMS m/z 521 $[M]^+$ (22), 449 (7), 350 (18), 334 (57), 248 (16), 234 (27), 196 (41), 182 (59), 180 (96), 178 (100), 166 (44), 154 (44); HREIMS m/z 521.2808 (calcd. for $C_{28}H_{43}NO_6S$, 521.2811).

Epothilone G, (10): colorless amorphous solid; $[\alpha]_D^{22}$ -39.7 (c 1.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 203 (15200), 236 (15100); IR (KBr) ν_{max} 3456, 2962, 2933, 2876, 1736,

1691, 1585, 1466, 1262, 980 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.47 (1H, s, H-19), 6.33 (1H, bs, H-17), 5.42 (1H, dd, J = 8.3, 2.9 Hz, H-15), 4.11 (1H, ddd, J = 10.1, 6.1, 3.4 Hz, H-3), 3.78 (1H, bddd, J = 5.2, 3.5, 3.5 Hz, H-7), 3.63 (1H, bd, J = 6.1 Hz, 3-OH), 3.21 (1H, dq, J = 5.2, 7.0 Hz, H-6), 3.00 (1H, ddd, J = 7.7, 4.8, 4.2 Hz, H-13), 2.88 (1H, ddd, J = 7.1, 4.2, 4.2 Hz, H-12), 2.53 (1H, dd, J = 14.8, 10.1 Hz, H-2a), 2.51 (1H, bd, J = 3.5 Hz, 7-OH), 2.43 (1H, dd, J = 14.8, 3.4 Hz, H-2b), 2.43 (3H, s, H-21), 2.07 (1H, ddd, J = 15.1, 4.8, 2.9 Hz, H-14a), 1.99 (3H, d, J = 1.3 Hz, H-27), 1.86 (1H, ddd, J = 15.1, 8.3, 7.7 Hz, H-14b), 1.71 (1H, m, H-8), 1.69 (1H, m, H-11a), 1.53 (1H, m, H-10a), 1.42 (1H, m, H-11b), 1.40 (3H, m, H-9 and H-10b), 1.34 (3H, s, H-23), 1.16 (3H, d, J = 7.0 Hz, H-24), 1.09 (3H, s, H-22), 0.99 (3H, d, J = 6.9 Hz, H-25); ^{13}C NMR (CDCl_3 , 100 MHz) δ 220.1 (s, C-5), 170.5 (s, C-1), 161.0 (s, C-20), 137.4 (s, C-18), 136.7 (s, C-16), 135.9 (d, C-19), 116.4 (d, C-17), 76.4 (d, C-15), 74.9 (d, C-7), 73.7 (d, C-3), 57.4 (d, C-12), 54.4 (d, C-13), 52.6 (s, C-4), 43.8 (d, C-6), 38.8 (t, C-2), 36.2 (d, C-8), 31.4 (t, C-14), 30.4 (t, C-9), 27.0 (t, C-11), 23.9 (t, C-10), 21.3 (q, C-23), 21.2 (q, C-22), 17.2 (q, C-25), 15.8 (q, C-27), 14.4 (q, C-24), 13.8 (q, C-21); EIMS m/z 477 $[\text{M}]^+$ (4), 405 (7), 290 (40), 152 (39), 150 (100), 148 (23), 124 (23); HREIMS m/z 477.2684 (calcd. for $\text{C}_{26}\text{H}_{39}\text{NO}_7$, 477.2727).

Epothilone G₂ (11): colorless amorphous solid; $[\alpha]_D^{22}$ -22.6 (c 1.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 202 (21500), 236 (14800); IR (KBr) ν_{max} 3456, 2965, 2934, 2877, 1737, 1690, 1586, 1464, 1250, 980 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.48 (1H, s, H-19), 6.33 (1H, bs, H-17), 5.43 (1H, dd, J = 7.1, 3.6 Hz, H-15), 4.12 (1H, ddd, J = 9.9, 6.4, 3.4 Hz, H-3), 3.77 (1H, ddd, J = 4.7, 4.4, 4.1 Hz, H-7), 3.83 (1H, bd, J = 6.4 Hz, 3-OH), 3.30 (1H, dq, J = 4.7, 6.9

Hz, H-6), 2.78 (1H, dd, $J = 7.0, 5.4$ Hz, H-13), 2.54 (1H, dd, $J = 14.3, 9.9$ Hz, H-2a), 2.51 (1H, bd, $J = 4.1$ Hz, 7-OH), 2.44 (3H, s, H-21), 2.40 (1H, dd, $J = 14.3, 3.4$ Hz, H-2b), 2.03 (1H, ddd, $J = 15.2, 5.4, 3.6$ Hz, H-14a), 2.00 (3H, d, $J = 1.3$ Hz, H-27), 1.92 (1H, ddd, $J = 15.1, 7.1, 7.0$ Hz, H-14b), 1.71 (1H, m, H-8), 1.68 (1H, m, H-11a), 1.51 (1H, m, H-10a), 1.42 (1H, m, H-11b), 1.39 (3H, m, H-9 and H-10b), 1.35 (3H, s, H-23), 1.26 (3H, s, H-26), 1.16 (3H, d, $J = 6.9$ Hz, H-24), 1.07 (3H, s, H-22), 0.99 (3H, d, $J = 7.0$ Hz, H-25); ^{13}C NMR (CDCl_3 , 100 MHz) δ 220.7 (s, C-5), 170.5 (s, C-1), 161.0 (s, C-20), 137.4 (s, C-18), 136.5 (s, C-16), 135.9 (d, C-19), 116.3 (d, C-17), 76.6 (d, C-15), 74.6 (d, C-7), 73.5 (d, C-3), 61.3 (s, C-12), 61.1 (d, C-13), 52.7 (s, C-4), 43.4 (d, C-6), 39.0 (t, C-2), 36.5 (d, C-8), 32.0 (t, C-11), 31.8 (t, C-14), 30.8 (t, C-9), 22.8 (t, C-10), 22.9 (q, C-26), 21.0 (q, C-23), 20.8 (q, C-22), 17.2 (q, C-25), 15.9 (q, C-27), 14.1 (q, C-24), 13.8 (q, C-21); EIMS m/z 491 [$\text{M}]^+$ (21), 419 (6), 320 (18), 304 (39), 166 (42), 152 (57), 150 (100), 149 (44), 148 (58), 124 (35), 109 (33); HREIMS m/z 491.2878 (calcd. for $\text{C}_{27}\text{H}_{41}\text{NO}_7$, 491.2883).

Epothilone H_1 (12): colorless amorphous solid; $[\alpha]_D^{22} -84.2$ (c 0.2, MeOH); UV (MeOH) λ_{max} nm (ϵ) 203 (19600), 237 (12000); IR (KBr) ν_{max} 3436, 2933, 2880, 2860, 1734, 1688, 1585, 1251, 1007 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.47 (1H, s, H-19), 6.31 (1H, bs, H-17), 5.43 (1H, ddd, $J = 10.6, 10.2, 4.5$ Hz, H-12), 5.36 (1H, dddd, $J = 10.6, 9.6, 5.0, 1.3$ Hz, H-13), 5.30 (1H, dd, $J = 9.9, 2.0$ Hz, H-15), 4.16 (1H, ddd, $J = 11.2, 5.3, 2.8$ Hz, H-3), 3.73 (1H, ddd, $J = 3.9, 2.5, 2.3$ Hz, H-7), 3.12 (1H, dq, $J = 2.3, 6.9$ Hz, H-6), 2.92 (1H, d, $J = 2.5$ Hz, 7-OH), 2.91 (1H, d, $J = 5.3$ Hz, 7-OH), 2.66 (1H, ddd, $J = 15.1, 9.9, 9.6$ Hz, H-14a), 2.50 (1H, dd, $J = 15.4, 11.2$ Hz, H-2a), 2.43 (3H, s, H-21), 2.37 (1H, dd, $J = 15.4, 2.8$ Hz, H-2b), 2.23

(1H, m, H-14b), 2.18 (1H, m, H-11a), 2.01 (1H, m, H-11b), 2.08 (3H, d, $J = 1.3$ Hz, H-27), 1.74 (1H, m, H-8), 1.65 (1H, m, H-10a), 1.33 (1H, m, H-9a), 1.31 (3H, s, H-23), 1.19 (1H, m, H-10b), 1.18 (1H, m, H-9b), 1.17 (3H, d, $J = 6.9$ Hz, H-24), 1.08 (3H, s, H-22), 0.99 (3H, d, $J = 7.1$ Hz, H-25); ^{13}C NMR, see Table 1; EIMS m/z 461 $[\text{M}]^+$ (6), 310 (5), 274 (10), 273 (7), 171 (63), 152 (100), 148 (18), 111 (15); HREIMS m/z 461.2743 (calcd. for $\text{C}_{26}\text{H}_{39}\text{NO}_6$, 461.2777).

Epothilone H_2 (13): colorless amorphous solid; $[\alpha]_D^{22} -44.4$ (c 0.25, MeOH); UV (MeOH) λ_{max} nm (ϵ) 203 (14500), 236 (12200); IR (KBr) ν_{max} 3436, 2967, 2935, 2880, 1734, 1690, 1586, 1251, 1007 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.46 (1H, s, H-19), 6.30 (1H, bs, H-17), 5.23 (1H, dd, $J = 9.8, 2.1$ Hz, H-15), 5.12 (1H, dd, $J = 10.1, 5.3$ Hz, H-13), 4.20 (1H, ddd, $J = 10.8, 5.7, 2.9$ Hz, H-3), 3.71 (1H, ddd, $J = 3.8, 2.6, 2.6$ Hz, H-7), 3.14 (1H, dq, $J = 2.6, 6.9$ Hz, H-6), 2.93 (d, $J = 5.7$ Hz, 3-OH), 2.90 (1H, bd, $J = 2.6$ Hz, 7-OH), 2.62 (1H, ddd, $J = 15.1, 9.8, 9.8$ Hz, H-14a), 2.46 (1H, dd, $J = 15.1, 10.8$ Hz, H-2a), 2.43 (3H, s, H-21), 2.32 (1H, dd, $J = 15.1, 2.9$ Hz, H-2b), 2.29 (1H, m, H-11a), 2.19 (1H, bd, $J = 15.1$ Hz, H-14b), 1.97 (3H, d, $J = 1.3$ Hz, H-27), 1.87 (1H, m, H-11b), 1.73 (1H, m, H-8), 1.67 (1H, m, H-10a), 1.65 (3H, bs, H-26), 1.32 (3H, s, H-23), 1.26 (2H, m, H-9), 1.24 (1H, m, H-10b), 1.18 (3H, d, $J = 6.9$ Hz, H-24), 1.07 (3H, s, H-22), 1.00 (3H, d, $J = 7.0$ Hz, H-25); ^{13}C NMR (CDCl_3 , 100 MHz) δ 220.6 (s, C-5), 170.3 (s, C-1), 161.0 (s, C-20), 138.6 (s, C-12), 138.4 (s, C-16), 137.5 (s, C-18), 135.6 (d, C-19), 120.8 (d, C-13), 115.8 (d, C-17), 78.9 (d, C-15), 74.3 (d, C-7), 72.7 (d, C-3), 53.3 (s, C-4), 42.0 (d, C-6), 39.6 (t, C-2), 38.6 (d, C-8), 32.4 (t, C-14), 31.9 (t, C-9), 31.6 (t, C-11), 25.6 (t, C-10), 23.0 (q, C-26), 22.8 (q, C-23), 18.8 (q, C-22), 16.1 (q, C-27), 15.9 (q, C-25), 13.8 (q, C-21), 13.6 (q, C-24); EIMS m/z 475 $[\text{M}]^+$ (11), 288 (9), 287 (5), 188 (7), 171 (32), 152 (100),

111 (10); HREIMS m/z 475.2913 (calcd. for $C_{27}H_{41}NO_6$, 475.2934).

Epothilone C₁ (16): colorless amorphous solid; $[\alpha]_D^{22}$ -114.0 (c 10.0, MeOH); UV (MeOH) λ_{\max} nm (ϵ) 211 (16500), 248 (12500); IR (KBr) ν_{\max} 3440, 2933, 2877, 2858, 1730, 1708, 1457, 1244, 981 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.96 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.47 (1H, dd, $J = 9.2, 3.0$ Hz, H-15), 5.43 (1H, m, H-12), 5.40 (1H, m, H-13), 4.40 (1H, ddd, $J = 6.2, 6.1, 6.1$ Hz, H-3), 3.69 (1H, dd, $J = 5.7, 3.6$ Hz, H-7), 3.01 (1H, dq, $J = 5.7, 6.9$ Hz, H-6), 3.01 (1H, bs, 3-OH), 2.84 (1H, dq, $J = 5.2, 7.0$ Hz, H-4), 2.68 (3H, s, H-21), 2.66 (1H, ddd, $J = 16.4, 9.2, 7.3$ Hz, H-14a), 2.64 (1H, dd, $J = 15.9, 7.1$ Hz, H-2a), 2.54 (1H, dd, $J = 15.9, 6.1$ Hz, H-2b), 2.38 (1H, bd, $J = 16.4$ Hz, H-14b), 2.35 (1H, bs, 7-OH), 2.07 (3H, bs, H-27), 2.03 (2H, m, H-11), 1.62 (1H, m, H-10a), 1.53 (1H, m, H-8), 1.35 (1H, m, H-9a), 1.22 (1H, m, H-9b), 1.19 (3H, d, $J = 6.9$ Hz, H-24), 1.14 (3H, d, $J = 6.9$ Hz, H-23), 1.10 (1H, m, H-10b), 0.95 (3H, d, $J = 6.9$ Hz, H-25); ^{13}C NMR, see Table 1; EIMS m/z 463 $[\text{M}]^+$ (5), 324 (8), 290 (8), 204 (7), 168 (100), 164 (15), 139 (36); HREIMS m/z 463.2381 (calcd. for $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$, 463.2392).

Epothilone D₁ (17): colorless amorphous solid; $[\alpha]_D^{22}$ -118.6 (c 0.5, MeOH); UV (MeOH) λ_{\max} nm (ϵ) 208 (18300), 249 (11900); IR (KBr) ν_{\max} 3439, 2965, 2934, 2877, 1729, 1707, 1456, 1250, 980 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.98 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.51 (1H, dd, $J = 9.5, 3.4$ Hz, H-15), 5.16 (1H, dd, $J = 8.0, 4.2$ Hz, H-13), 4.42 (1H, ddd, $J = 7.1, 6.3, 5.5$ Hz, H-3), 3.70 (1H, dd, $J = 6.5, 2.9$ Hz, H-7), 3.07 (1H, dq, $J = 6.5, 6.9$ Hz, H-6), 2.95 (1H, dq, $J = 4.7, 7.0$ Hz, H-4), 2.71 (3H, s, H-21), 2.69 (1H, dd, $J = 16.0, 6.3$ Hz, H-2a), 2.64 (1H, m, H-14a), 2.59 (1H, dd, $J = 16.0, 7.1$ Hz, H-2b), 2.46 (1H, bs, 3-OH), 2.38 (1H, bd, $J = 16.0$ Hz, H-14b), 2.19 (1H, ddd, $J = 13.3, 8.6, 5.7$ Hz, H-11a), 2.10 (3H, d, $J = 1.4$ Hz, H-27), 2.02 (1H, bs, 7-OH), 1.91 (1H, ddd, $J = 13.3, 6.0, 6.0$ Hz, H-11b), 1.68 (1H, m, H-10a), 1.66 (3H, bs, H-26), 1.53 (1H, m, H-8), 1.37 (1H, m, H-9a), 1.26 (1H, m, H-9b), 1.24 (3H, d, $J = 6.9$ Hz, H-24), 1.19 (1H, m, H-10b), 1.14 (3H, d, $J = 7.0$, H-23), 0.99 (3H, d, $J = 6.9$ Hz, H-25); ^{13}C NMR (CDCl_3 , 100 MHz) δ 217.0 (s, C-5), 169.7 (s, C-1), 165.0 (s, C-20), 152.2 (s, C-18), 138.5 (s, C-12), 137.7 (s, C-16), 120.7 (d, C-13), 120.1 (d, C-17), 116.3 (d, C-19), 78.8 (d, C-15), 77.2 (d, C-7), 67.7 (d, C-3), 52.1 (d, C-4), 46.5 (d, C-6), 40.6 (t, C-2), 37.6 (d, C-8), 32.3 (t, C-14), 31.8 (t, C-11), 29.5 (t, C-9), 25.5 (t, C-10), 23.1 (q, C-26), 19.2 (q, C-21), 15.5 (q, C-27), 16.6 (q, C-25), 14.5 (q, C-24), 9.7 (q, C-23); EIMS m/z 477 $[\text{M}]^+$ (13), 304 (19), 303 (31), 218 (40), 204 (41), 163 (100), 164 (45), 157 (25), 139 (18); HREIMS m/z 477.2544 (calcd. for $\text{C}_{26}\text{H}_{39}\text{NO}_5\text{S}$, 477.2549).

Epothilone C₂ (18): colorless amorphous solid; $[\alpha]_D^{22}$ -11.6 (c 10.0, MeOH); UV (MeOH) λ_{\max} nm (ϵ) 212 (15500), 249 (12100); IR (KBr) ν_{\max} 3428, 2962, 2929, 2877, 2859, 1734, 1705, 1460, 1251, 982 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.99 (1H, s, H-19), 6.66 (1H,

bs, H-17), 5.55 (1H, ddd, $J = 10.4, 9.2, 6.1$ Hz, H-12), 5.38 (1H, ddd, $J = 10.4, 9.3, 6.2$ Hz, H-13), 5.22 (1H, dd, $J = 8.8, 2.8$ Hz, H-15), 4.42 (1H, dddd, $J = 9.4, 5.6, 4.2, 4.1$ Hz, H-3), 3.93 (1H, d, $J = 5.6$ Hz, 3-OH), 3.86 (1H, m, H-7), 3.15 (1H, bs, 7-OH), 3.12 (1H, dq, $J = 4.2, 7.0$ Hz, H-4), 3.00 (1H, dq, $J = 6.9, 7.0$ Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dddd, $J = 15.1, 9.3, 8.8, 0.8$ Hz, H-14a), 2.58 (1H, dd, $J = 15.4, 9.4$ Hz, H-2a), 2.38 (1H, dd, $J = 15.4, 4.1$ Hz, H-2b), 2.31 (1H, ddd, $J = 15.1, 6.2, 2.8$ Hz, H-14b), 2.08 (3H, d, $J = 1.3$ Hz, H-27), 2.15 (1H, m, H-11a), 2.04 (1H, m, H-11b), 1.71 (1H, m, H-8), 1.59 (1H, m, H-10a), 1.43 (1H, m, H-9a), 1.31 (1H, m, H-9b), 1.26 (3H, d, $J = 7.0$ Hz, H-24), 1.15 (3H, d, $J = 7.0$ Hz, H-23), 1.11 (1H, m, H-10b), 1.00 (3H, d, $J = 6.9$ Hz, H-25); ^{13}C NMR, see Table 1; EIMS m/z 463 $[\text{M}]^+$ (7), 324 (7), 306 (8), 290 (17), 168 (100), 164 (14), 139 (27); HREIMS m/z 463.2392 (calcd. for $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$, 463.2392).

Epithilone D: (19): colorless amorphous solid; $[\alpha]_D^{22} -12.5$ (c 1.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 210 (15400), 248 (11200); IR (KBr) ν_{max} 3436, 2965, 2930, 2877, 1732, 1705, 1458, 1253, 980 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.97 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.18 (1H, dd, $J = 7.9, 4.9$ Hz, H-15), 5.18 (1H, ddd, $J = 9.6, 5.4, 1.0$ Hz, H-13), 4.27 (1H, m, H-3), 3.88 (1H, dd, $J = 5.6, 4.6$ Hz, H-7), 3.19 (1H, bs, 3-OH), 3.07 (1H, dq, $J = 4.3, 7.0$ Hz, H-4), 2.95 (1H, dq, $J = 5.6, 7.0$ Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dd, $J = 14.9, 7.8$ Hz, H-2a), 2.56 (1H, ddd, $J = 14.7, 9.6, 7.9$ Hz, H-14a), 2.43 (1H, dd, $J = 14.9, 5.6$ Hz, H-2b), 2.38 (1H, bs, 7-OH), 2.26 (1H, ddd, $J = 14.5, 5.4, 4.9$ Hz, H-14b), 2.19 (1H, ddd, $J = 13.0, 10.4, 5.4$ Hz, H-11a), 2.10 (3H, d, $J = 1.4$ Hz, H-27), 1.95 (1H, ddd, $J = 13.0, 10.3, 5.3$ Hz, H-11b), 1.72 (1H, m, H-8), 1.68 (3H, bs, H-26), 1.61 (1H, m, H-10a), 1.39 (2H, m, H-9), 1.21 (1H, m, H-10b).

1.19 (3H, d, $J = 6.9$ Hz, H-24), 1.17 (3H, d, $J = 7.0$, H-22), 1.00 (3H, d, $J = 6.9$ Hz, H-25); ^{13}C NMR (CDCl_3 , 100 MHz) δ 216.8 (s, C-5), 170.4 (s, C-1), 164.9 (s, C-20), 152.3 (s, C-18), 139.8 (s, C-12), 137.5 (s, C-16), 120.5 (d, C-17), 119.2 (d, C-13), 116.3 (d, C-19), 80.0 (d, C-15), 74.3 (d, C-7), 69.7 (d, C-3), 48.6 (d, C-4), 48.4 (d, C-6), 39.9 (t, C-2), 36.6 (d, C-8), 32.2 (t, C-14), 32.7 (t, C-11), 30.9 (t, C-9), 26.0 (t, C-10), 23.6 (q, C-26), 19.2 (q, C-21), 15.4 (q, C-27), 17.1 (q, C-25), 12.4 (q, C-24), 12.7 (q, C-23); EIMS m/z 477 $[\text{M}]^+$ (22), 304 (19), 303 (17), 218 (22), 204 (25), 168 (100), 164 (28), 157 (31), 139 (21); HREIMS m/z 477.2545 (calcd. for $\text{C}_{26}\text{H}_{39}\text{NO}_5\text{S}$, 477.2549).

Epithilone C₃ (20): colorless amorphous solid; $[\alpha]_D^{22} -62.1$ (c 5.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 212 (16200), 248 (12300); IR (KBr) ν_{max} 3432, 2928, 2878, 2858, 1736, 1698, 1252, 1040 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.95 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.44 (1H, ddd, $J = 10.9, 10.3, 5.4$ Hz, H-12), 5.33 (1H, ddd, $J = 10.9, 9.3, 4.6$ Hz, H-13), 5.23 (1H, dd, $J = 9.5, 2.2$ Hz, H-15), 4.36 (1H, ddd, $J = 11.3, 5.6, 2.3$ Hz, H-3), 4.04 (1H, d, $J = 5.6$ Hz, 3-OH), 3.93 (1H, ddd, $J = 9.5, 2.3, 1.4$ Hz, H-7), 3.56 (1H, bd, $J = 2.3$ Hz, 7-OH), 2.70 (1H, dd, $J = 18.0, 1.4$ Hz, H-6a), 2.67 (3H, s, H-21), 2.61 (1H, ddd, $J = 15.3, 9.5, 9.3$ Hz, H-14a), 2.38 (1H, dd, $J = 14.3, 11.3$ Hz, H-2a), 2.36 (1H, dd, $J = 18.0, 9.5$ Hz, H-6b), 2.28 (1H, bd, $J = 15.3$ Hz, H-14b), 2.12 (1H, m, H-11a), 2.06 (1H, dd, $J = 14.3, 2.3$ Hz, H-2b), 2.03 (3H, d, $J = 1.3$ Hz, H-27), 1.96 (1H, m, H-11b), 1.75 (1H, m, H-8), 1.54 (1H, m, H-10a), 1.26 (1H, m, H-9a), 1.25 (3H, s, H-23), 1.17 (1H, m, H-10b), 1.15 (1H, m, H-9b), 1.03 (3H, s, H-22), 0.91 (3H, d, $J = 6.8$ Hz, H-25); ^{13}C NMR, see Table 1; EIMS m/z 463 $[\text{M}]^+$ (28), 290 (14), 168 (100), 164 (36), 157 (44), 151 (25); HREIMS m/z 463.2379 (calcd. for $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$, 463.2392).

Epothilone C₄ (21): colorless amorphous solid; $[\alpha]_D^{22}$ -75.6 (c 1.0, MeOH); UV (MeOH) λ_{\max} nm (ϵ) 212 (17200), 248 (12500); IR (KBr) ν_{\max} 3434, 2974, 2932, 2859, 1735, 1686, 1252, 1046 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.96 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.43 (1H, m, H-12), 5.40 (1H, m, H-13), 5.26 (1H, dd, J = 9.6, 2.3 Hz, H-15), 4.41 (1H, ddd, J = 11.4, 5.8, 2.5 Hz, H-3), 3.78 (1H, m, H-7), 3.70 (1H, bs, 3-OH), 3.46 (1H, d, J = 0.9 Hz, 7-OH), 3.01 (1H, dq, J = 0.5, 7.0 Hz, H-6), 2.69 (3H, s, H-21), 2.66 (1H, ddd, J = 15.3, 9.6, 8.8 Hz, H-14a), 2.47 (1H, dd, J = 14.5, 11.4 Hz, H-2a), 2.29 (1H, m, H-14b), 2.25 (1H, dd, J = 14.5, 2.5 Hz, H-2b), 2.24 (1H, m, H-11a), 2.07 (3H, d, J = 1.4 Hz, H-27), 1.96 (1H, m, H-11b), 1.51 (2H, m, H-8), 1.44 (2H, m, H-10), 1.37 (2H, m, H-9), 1.32 (3H, s, H-23), 1.17 (3H, d, J = 7.0 Hz, H-24), 1.07 (3H, s, H-22); ^{13}C NMR, see Table 1; EIMS m/z 463 $[\text{M}]^+$ (7), 276 (15), 171 (33), 168 (100), 164 (23), 151 (22), 111 (13); HREIMS m/z 463.2373 (calcd. for $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$, 463.2392).

Epothilone C₅ (22): colorless amorphous solid; $[\alpha]_D^{22}$ -158.2 (c 0.5, MeOH); UV (MeOH) λ_{\max} nm (ϵ) 205 (19500), 247 (12700); IR (KBr) ν_{\max} 3447, 2972, 2927, 1737, 1690, 1450, 1252, 1181, 986 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.93 (1H, s, H-19), 6.48 (1H, bs, H-17), 5.48 (1H, ddd, J = 10.7, 6.2, 6.2 Hz, H-12), 5.39 (1H, m, H-13), 5.37 (1H, m, H-9), 5.34 (1H, dd, J = 8.0, 2.3 Hz, H-15), 4.29 (1H, dd, J = 6.0, 2.6 Hz, H-7), 4.09 (1H, ddd, J = 10.8, 7.1, 2.9 Hz, H-3), 3.59 (1H, d, J = 7.1 Hz, 3-OH), 3.17 (1H, dq, J = 6.0, 6.9 Hz, H-6), 2.68 (3H, s, H-21), 2.54 (1H, ddd, J = 15.2, 8.1, 8.0 Hz, H-14a), 2.44 (1H, bs, 7-OH), 2.42 (1H, dd, J = 15.1, 2.9 Hz, H-2a), 2.41 (1H, ddd, J = 15.2, 2.3, 2.3 Hz, H-14b), 2.34 (1H, dd, J = 15.1, 10.8 Hz, H-2b), 2.20 (1H, m, H-10a), 2.18 (2H, m, H-11), 2.12 (1H, m, H-10b), 2.06 (3H, bs, H-27), 1.67 (3H, bs, H-25), 1.27 (3H, s, H-23), 1.21 (3H, d, J = 6.9 Hz, H-24), 1.15 (3H, s, H-22); ^{13}C NMR,

see Table 1; EIMS m/z 475 $[M]^+$ (6), 392 (7), 304 (6), 288 (33), 204 (76), 171 (19), 168 (100), 164 (12); HREIMS m/z 475.2380 (calcd. for $C_{26}H_{37}NO_5S$, 475.2392).

Epothilone D₅ (23): colorless amorphous solid; $[\alpha]_D^{22}$ -150 (*c* 0.2, MeOH); UV (MeOH) λ_{max} nm (ϵ) 205 (23300), 248 (13600); IR (KBr) ν_{max} 3439, 2967, 2927, 1736, 1690, 1451, 1254, 1181, 987 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ : 6.94 (1H, s, H-19), 6.51 (1H, bs, H-17), 5.34 (1H, bs, H-9), 5.29 (1H, dd, J = 8.0, 2.4 Hz, H-15), 5.16 (1H, dd, J = 8.2, 6.2 Hz, H-13), 4.30 (1H, bd, J = 4.9 Hz, H-7), 4.19 (1H, ddd, J = 10.8, 7.6, 3.0 Hz, H-3), 3.68 (1H, d, J = 7.6 Hz, 3-OH), 3.17 (1H, dq, J = 4.9, 7.0 Hz, H-6), 2.69 (3H, s, H-21), 2.65 (1H, d, J = 2.1 Hz, 7-OH), 2.56 (1H, ddd, J = 16.2, 8.2, 8.0 Hz, H-14a), 2.40 (1H, dd, J = 15.0, 3.0 Hz, H-2a), 2.39 (1H, bd, J = 16.2 Hz, H-14b), 2.34 (1H, dd, J = 15.0, 10.8 Hz, H-2b), 2.25 (2H, m, H-10a and H-11a), 2.20 (1H, m, H-10b), 2.17 (1H, m, H-11b), 2.05 (3H, d, J = 1.0 Hz, H-27), 1.69 (3H, bs, H-25), 1.68 (3H, bs, H-26), 1.29 (3H, s, H-23), 1.23 (3H, d, J = 7.0 Hz, H-24), 1.16 (3H, s, H-22); ^{13}C NMR, see Table 1; EIMS m/z 489 $[M]^+$ (4), 406 (4), 338 (7), 302 (13), 218 (35), 171 (10), 168 (100), 153 (20), 125 (10); HREIMS m/z 489.2536 (calcd. for $C_{27}H_{39}NO_5S$, 489.2549).

Epothilone C₆ (24): colorless amorphous solid; $[\alpha]_D^{22}$ -205.2 (*c* 1.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 218 (24600), 237 (28800); IR (KBr) ν_{max} 3435, 2967, 2927, 2882, 1732, 1688, 1465, 1258, 988 cm^{-1} ; 1H NMR ($CDCl_3$, 300 MHz) δ : 6.97 (1H, s, H-19), 6.58 (1H, bs, H-17), 6.43 (1H, dd, 15.5, 10.8 Hz, H-11), 6.11 (1H, dd, J = 10.8, 10.6 Hz, H-12), 5.75 (1H, ddd, J = 15.5, 8.3, 5.6 Hz, H-10), 5.34 (1H, m, H-13), 5.34 (1H, dd, J = 9.7, 2.4 Hz, H-15), 4.16 (1H, ddd, J = 9.2, 4.9, 4.3 Hz, H-3), 3.74 (1H, ddd, J = 2.2, 2.1, 1.7 Hz, H-7), 3.24 (1H, dq, J = 2.1, 6.9 Hz, H-6), 3.06 (1H, d, J = 2.2 Hz, 7-OH), 2.93 (1H, d, J = 4.9 Hz, 3-OH), 2.78 (1H, dddd,

$J = 14.1, 9.9, 9.7, 0.7$, H-14a), 2.71 (3H, s, H-21), 2.48 (1H, m, H-9a), 2.47 (1H, dd, $J = 15.5$, 9.2 Hz, H-2a), 2.40 (1H, dd, $J = 15.5$, 4.3 Hz, H-2b), 2.38 (1H, bdd, $J = 14.1$, 7.8 Hz, H-14b), 2.11 (3H, d, $J = 1.3$ Hz, H-27), 1.96 (1H, m, H-8), 1.33 (3H, s, H-23), 1.11 (3H, d, $J = 6.9$ Hz, H-24), 1.06 (3H, s, H-22), 1.05 (3H, d, $J = 6.8$ Hz, H-25); ^{13}C NMR, see Table 1; EIMS m/z 475 $[\text{M}]^+$ (13), 387 (2), 316 (4), 288 (15), 230 (16), 204 (9), 171 (18), 168 (100), 164 (14), 151 (17); HREIMS m/z 475.2361 (calcd. for $\text{C}_{26}\text{H}_{37}\text{NO}_5\text{S}$, 475.2392).

Epithilone C₇ (25): colorless amorphous solid; $[\alpha]_D^{25} -\text{XXX}$ (c 2.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) XXX (XXX), XXX (XXX); IR (KBr) ν_{max} XXX cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.01 (1H, s, H-19), 6.66 (1H, bs, H-17), 5.59 (1H, ddd, $J = 11.1, 11.1, 3.8$ Hz, H-12), 5.40 (1H, dd, $J = 11.1, 9.2$, H-13), 5.03 (1H, d, $J = 9.3$ Hz, H-15), 4.62 (1H, dd, $J = 9.3, 9.2$ Hz, H-14), 4.18 (1H, bd, $J = 11.0$ Hz, H-3), 3.72 (1H, bs, H-7), 3.20 (1H, bs, 3-OH), 3.09 (1H, dq, $J = 1.9, 6.8$ Hz, H-6), 3.00 (1H, bs, 7-OH), 2.69 (3H, s, H-21), 2.47 (1H, dd, $J = 14.8, 11.0$ Hz, H-2a), 2.32 (1H, dd, $J = 14.8, 2.6$ Hz, H-2b), 2.27 (1H, m, H-11a), 2.19 (3H, bs, H-27), 2.13 (1H, m, H-11b), 1.76 (1H, m, H-8), 1.70 (1H, m, H-10a), 1.35 (1H, m, H-9a), 1.32 (3H, s, H-23), 1.23 (1H, m, H-9b), 1.21 (1H, m, H-10b), 1.18 (3H, d, $J = 6.8$ Hz, H-24), 1.08 (3H, s, H-22), 1.00 (3H, d, $J = 6.9$ Hz, H-25); EIMS m/z 493 $[\text{M}]^+$ XXX; HREIMS m/z 493.XXX (calcd. for $\text{C}_{26}\text{H}_{39}\text{NO}_6\text{S}$, 493.2498).

Epithilone C₈ (26): colorless amorphous solid; $[\alpha]_D^{25} -75.2$ (c 2.5, MeOH); UV (MeOH) λ_{max} nm (ϵ) 210 (16800), 248 (17800); IR (KBr) ν_{max} 3443, 2932, 2881, 1734, 1689, 1465, 1255, 1183, 976 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.93 (1H, s, H-19), 6.62 (1H, dd, $J = 15.6, 0.6$ Hz, H-17), 6.49 (1H, dd, $J = 15.6, 6.6$ Hz, H-16), 5.52 (1H, dddd, $J = 9.5, 6.6, 2.8, 0.6$ Hz, H-

15), 5.42 (1H, m, H-12), 5.41 (1H, m, H-13), 4.13 (1H, ddd, $J = 11.0, 5.3, 2.8$ Hz, H-3), 3.69 (1H, ddd, $J = 3.7, 2.8, 2.5$ Hz, H-7), 3.11 (1H, dq, $J = 2.5, 6.8$ Hz, H-6), 2.95 (1H, d, $J = 5.3$ Hz, 3-OH), 2.90 (1H, d, $J = 2.8$ Hz, 7-OH), 2.69 (3H, s, H-21), 2.67 (1H, ddd, $J = 14.9, 9.5, 8.4$ Hz, H-14a), 2.48 (1H, dd, $J = 15.6, 11.0$ Hz, H-2a), 2.33 (1H, dd, $J = 15.6, 2.8$ Hz, H-2b), 2.30 (1H, bd, $J = 14.9$ Hz, H-14b), 2.14 (1H, m, H-11a), 2.03 (1H, m, H-11b), 1.71 (1H, m, H-8), 1.63 (1H, m, H-10a), 1.31 (1H, m, H-9a), 1.29 (3H, s, H-23), 1.17 (3H, d, $J = 6.8$ Hz, H-24), 1.16 (1H, m, H-10b), 1.14 (1H, m, H-9b), 1.05 (3H, s, H-22), 0.97 (3H, d, $J = 7.1$ Hz, H-25); ^{13}C NMR, see Table 1; EIMS m/z 463 $[\text{M}]^+$ (21), 310 (10), 276 (21), 171 (83), 154 (100), 150 (27), 111 (18); HREIMS m/z 463.2382 (calcd. for $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$, 463.2392).

Epothilone C₉ (27): colorless amorphous solid; $[\alpha]_D^{25} -93.4$ (c 1.0, MeOH); UV (MeOH) λ_{max} nm (ϵ) 209 (15200), 254 (15700); IR (KBr) ν_{max} 3416, 2966, 2932, 1736, 1689, 1463, 1249, 1011 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 7.06 (1H, s, H-19), 6.65 (1H, bs, H-17), 6.56 (1H, dd, $J = 10.6, 4.4$ Hz, 27-OH), 5.55 (1H, d, $J = 6.2$ Hz, 3-OH), 5.52 (1H, dd, $J = 11.6, 2.0$ Hz, H-15), 5.44 (1H, dddd, $J = 11.2, 10.7, 3.1, 1.7$ Hz, H-12), 5.35 (1H, dddd, $J = 11.0, 10.7, 3.9, 1.7$ Hz, H-13), 4.47 (1H, ddd, $J = 12.5, 4.4, 1.3$ Hz, H-27a), 4.35 (1H, ddd, $J = 11.7, 6.2, 2.6$ Hz, H-3), 4.20 (1H, ddd, $J = 12.5, 10.6, 0.9$ Hz, H-27b), 3.63 (1H, ddd, $J = 4.6, 1.8, 0.9$ Hz, H-7), 3.24 (1H, d, $J = 1.8$ Hz, 7-OH), 3.13 (1H, dq, $J = 0.9, 6.8$ Hz, H-6), 2.80 (1H, ddd, $J = 14.8, 11.6, 11.0$ Hz, H-14a), 2.71 (3H, s, H-21), 2.40 (1H, dd, $J = 14.4, 11.7$ Hz, H-2a), 2.24 (1H, m, H-11a), 2.06 (1H, dd, $J = 14.4, 2.6$ Hz, H-2b), 2.01 (1H, ddd, $J = 14.8, 3.9, 2.0$ Hz, H-14b), 2.00 (1H, m, H-11b), 1.77 (1H, m, H-8), 1.69 (1H, m, H-10a), 1.35 (1H, m, H-9a), 1.35 (3H, s, H-23), 1.19 (1H, m, H-10b), 1.19 (3H, d, $J = 6.8$ Hz, H-24), 1.18 (1H, m, H-9b), 1.01 (3H, d, $J =$

7.1 Hz, H-25), 0.98 (3H, s, H-22); ^{13}C NMR, see Table 1; EIMS m/z 493 $[\text{M}]^+$ (17), 306 (64), 184 (50), 171 (30), 167 (38), 166 (100), 138 (12); HREIMS m/z 493.2502 (calcd. for $\text{C}_{26}\text{H}_{39}\text{NO}_6\text{S}$, 493.2498).

trans-Epothilone C₁ (28): colorless amorphous solid; $[\alpha]_D^{22}$ -84 (*c* 0.2, MeOH); UV (MeOH) λ_{max} nm (ϵ) 211 (17400), 248 (12900); IR (KBr) ν_{max} 3433, 2961, 2933, 2879, 1730, 1708, 1457, 1251, 975 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 7.00 (1H, s, H-19), 6.64 (1H, bs, H-17), 5.45 (1H, ddd, J = 15.2, 6.5, 6.5 Hz, H-12), 5.42 (1H, dd, J = 6.4, 3.7 Hz, H-15), 5.35 (1H, dt, J = 15.2, 7.1 Hz, H-13), 4.42 (1H, m, H-3), 3.58 (1H, ddd, J = 8.1, 7.9, 2.8 Hz, H-7), 3.24 (1H, m, H-6), 3.14 (1H, dq, J = 4.0, 6.9 Hz, H-6), 2.92 (1H, d, J = 7.9 Hz, 7-OH), 2.71 (3H, s, H-21), 2.71 (2H, m, H-2), 2.53 (2H, m, H-14), 2.17 (1H, d, J = 2.17 Hz, 3-OH), 2.11 (1H, m, H-11a), 2.06 (3H, bs, H-27), 1.93 (1H, m, H-11b), 1.68 (1H, m, H-9a), 1.65 (1H, m, H-10a), 1.33 (1H, m, H-8), 1.26 (3H, d, J = 6.8 Hz, H-24), 1.16 (1H, m, H-10b), 1.12 (3H, d, J = 6.9 Hz, H-22), 1.07 (1H, m, H-9b), 1.00 (3H, d, J = 6.8 Hz, H-25); ^{13}C NMR, see Table 1; EIMS m/z 463 $[\text{M}]^+$ (6), 290 (21), 289 (20), 204 (23), 194 (19), 190 (22), 168 (100), 164 (48), 157 (14), 152 (19), 151 (17), 139 (15), 111 (18); HREIMS m/z 463.2371 (calcd. for $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$, 463.2392).

trans-Epothilone C₂ (29): colorless amorphous solid; $[\alpha]_D^{22}$ -3 (*c* 1.5, MeOH); UV (MeOH) λ_{max} nm (ϵ) 211 (15800), 248 (11900); IR (KBr) ν_{max} 3435, 2963, 2931, 2878, 1731, 1706, 1457, 1273, 979 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ 6.99 (1H, s, H-19), 6.57 (1H, bs, H-17), 5.56 (1H, ddd, J = 15.1, 7.4, 7.0 Hz, H-12), 5.41 (1H, ddd, J = 15.1, 7.0, 6.9 Hz, H-13), 5.41 (1H, dd, J = 7.7, 2.8 Hz, H-15), 4.13 (1H, dddd, J = 6.7, 6.2, 5.6, 5.1 Hz, H-3), 3.78 (1H, ddd, J = 8.2, 6.5, 1.9 Hz, H-7), 3.18 (1H, d, J = 5.6 Hz, 3-OH), 3.06 (1H, dq, J = 8.2, 7.1 Hz,

H-6), 2.98 (1H, dq, $J = 6.2, 7.0$ Hz, H-4), 2.71 (3H, s, H-21), 2.64 (1H, dd, $J = 15.1, 6.7$ Hz, H-2a), 2.54 (1H, dd, $J = 15.1, 5.1$ Hz, H-2b), 2.44 (2H, m, H-14), 2.22 (1H, dddd, $J = 13.8, 7.0, 6.2, 2.9$ Hz, H-11a), 2.10 (3H, d, $J = 1.1$ Hz, H-27), 2.09 (1H, d, $J = 6.5$ Hz, 7-OH), 1.88 (1H, dddd, $J = 13.8, 10.9, 7.4, 2.9$ Hz, H-11b), 1.65 (1H, m, H-8), 1.63 (1H, m, H-10a), 1.56 (1H, dddd, $J = 12.7, 12.7, 3.9, 3.9$ Hz, H-9a), 1.20 (3H, d, $J = 7.1$ Hz, H-24), 1.15 (3H, d, $J = 7.0$ Hz, H-23), 1.13 (1H, m, H-10b), 1.04 (1H, m, H-9b), 1.01 (3H, d, $J = 7.0$ Hz, H-25); ^{13}C NMR, see Table 1; EIMS m/z 463 $[\text{M}]^+$ (13), 290 (11), 190 (10), 168 (100), 164 (20), 157 (26), 139 (17); HREIMS m/z 463.2383 (calcd. for $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$, 463.2392).

Epothilone I₁ (30): colorless amorphous solid; $[\alpha]_D^{25}$ -XXX (c XXX, MeOH); UV (MeOH) λ_{max} nm (ϵ) XXX; IR (KBr) ν_{max} XXX cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.96 (1H, s, H-19), 6.54 (1H, bs, H-17), 5.49 (1H, ddd, $J = 10.3, 7.3, 7.3$ Hz, H-12), 5.33 (1H, dd, $J = 8.3, 4.4$ Hz, H-15), 5.31 (1H, m, H-13), 4.15 (1H, ddd, $J = 8.0, 5.0, 4.6$ Hz, H-3), 3.80 (1H, m, H-7), 3.21 (1H, dq, $J = 6.0, 6.9$ Hz, H-6), 2.89 (1H, d, $J = 5.0$ Hz, 3-OH), 2.70 (3H, s, H-21), 2.65 (1H, ddd, $J = 15.8, 8.5, 8.3$ Hz, H-14a), 2.42 (2H, m, H-2), 2.35 (1H, m, H-14b), 2.27 (1H, bd, $J = 3.3$ Hz, 7-OH), 2.13 (1H, m, H-11a), 2.09 (3H, d, $J = 1.2$ Hz, H-27), 2.00 (1H, m, H-11b), 1.72 (1H, m, H-8), 1.40 (2H, m, H-10_p), 1.37 (1H, m, H-9_pa), 1.36 (2H, m, H-9_a), 1.32 (3H, s, H-23), 1.27 (3H, m, H-9_pb and H-10_a), 1.13 (3H, d, $J = 6.9$ Hz, H-24), 1.09 (3H, s, H-22), 0.94 (3H, d, $J = 6.9$ Hz, H-25); ^{13}C NMR (CDCl_3 , 75 MHz) δ 221.3 (s, C-5), 171.1 (s, C-1), 164.8 (s, C-20), 152.4 (s, C-18), 137.4 (s, C-16), 133.8 (d, C-12), 124.6 (d, C-13), 120.0 (d, C-17), 116.2 (d, C-19), 78.8 (d, C-15), 74.9 (d, C-7), 74.7 (d, C-3), 51.6 (s, C-4), 43.7 (d, C-6), 38.9 (t, C-2), 34.3 (d, C-8), 31.6 (t, C-14), 29.3 (t, C-9_a), 28.6 (t, C-10_p), 28.2 (t, C-10_a), 26.6 (t, C-

11), 24.8 (t, C-9_β), 23.6 (q, C-22), 19.3 (q, C-23), 19.3 (q, C-21), 16.5 (q, C-25), 15.5 (q, C-27), 13.7 (q, C-24); EIMS m/z 505 [M]⁺ XXX; HREIMS m/z 505.XXX (calcd. for C₂₈H₄₃NO₅S, 505.XXX).

Epothilone I₂ (31): colorless amorphous solid; $[\alpha]_D^{22}$ -XXX (c XXX, MeOH); UV (MeOH) λ_{\max} nm (ε) XXX; IR (KBr) ν_{\max} XXX cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 6.95 (1H, s, H-19), 6.53 (1H, bs, H-17), 5.40 (1H, m, H-12), 5.38 (1H, dd, J = 9.8, 3.3 Hz, H-15), 5.37 (1H, m, H-13), 4.21 (1H, ddd, J = 8.6, 3.8, 3.6 Hz, H-3), 3.85 (1H, ddd, J = 8.5, 5.8, 2.2 Hz, H-7), 3.18 (1H, dq, J = 8.5, 7.0 Hz, H-6), 2.70 (3H, s, H-21), 2.65 (1H, ddd, J = 15.2, 9.8, 9.0 Hz, H-14a), 2.51 (1H, d, J = 3.6 Hz, 3-OH), 2.37 (2H, m, H-2), 2.32 (1H, bd, J = 15.2 Hz, H-14b), 2.09 (3H, d, J = 1.3 Hz, H-27), 2.07 (2H, m, H-11), 1.78 (1H, m, H-8), 1.65 (1H, d, J = 5.8 Hz, 7-OH), 1.57 (1H, m, H-10_βa), 1.44 (1H, m, H-10_αa), 1.42 (1H, m, H-9_β), 1.32 (3H, s, H-23), 1.21 (1H, m, H-10_βb), 1.17 (3H, d, J = 7.0 Hz, H-24), 1.13 (2H, m, H-9_α), 1.06 (3H, s, H-22), 0.95 (3H, d, J = 7.0 Hz, H-25_α), 0.91 (3H, d, J = 6.5 Hz, H-25_β), 0.68 (1H, m, H-10_αb); ¹³C NMR (CDCl₃, 100 MHz) δ 220.4 (s, C-5), 171.3 (s, C-1), XXX (s, C-20), 152.4 (s, C-18), 137.6 (s, C-16), 134.5 (d, C-12), 125.3 (d, C-13), 119.6 (d, C-17), 116.2 (d, C-19), 78.6 (d, C-15), 77.2 (d, C-7), 75.0 (d, C-3), 51.0 (s, C-4), 44.6 (d, C-6), 38.2 (t, C-2), 36.9 (t, C-9_α), 34.5 (t, C-10_α), 32.6 (d, C-8), 32.0 (t, C-14), 30.0 (d, C-9_β), 27.4 (t, C-11), 26.6 (t, C-10_β), 25.0 (q, C-22), 21.5 (q, C-25_β), 19.3 (q, C-21), 17.9 (q, C-25_α), 17.7 (q, C-23), 15.8 (q, C-24), 15.6 (q, C-27); EIMS m/z 519 [M]⁺ XXX; HREIMS m/z 519.XXX (calcd. for C₂₉H₄₅NO₅S, 519.XXX).

Epothilone I₃ (32): colorless amorphous solid; $[\alpha]_D^{22}$ -XXX (c XXX, MeOH); UV (MeOH) λ_{\max} nm (ε) XXX; IR (KBr) ν_{\max} XXX cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 6.95 (1H,

s, H-19), 6.52 (1H, bs, H-17), 5.32 (1H, dd, $J = 9.1, 3.0$ Hz, H-15), 5.08 (1H, dd, $J = 8.5, 3.9$ Hz, H-13), 4.13 (1H, ddd, $J = 9.4, 4.3, 3.2$ Hz, H-3), 3.81 (1H, m, H-7), 3.18 (1H, dq, $J = 6.8, 7.0$ Hz, H-6), 2.83 (1H, d, $J = 4.3$ Hz, 3-OH), 2.70 (3H, s, H-21), 2.61 (1H, ddd, $J = 15.8, 9.1, 8.5$ Hz, H-14a), 2.43 (1H, dd, $J = 14.0, 3.2$ Hz, H-2a), 2.38 (2H, dd, $J = 14.0, 9.4$ Hz, H-2b), 2.30 (1H, bd, $J = 15.8$ Hz, H-14b), 2.16 (1H, ddd, $J = 14.1, 8.3, 7.4$ Hz, H-11a), 2.08 (3H, d, $J = 1.0$ Hz, H-27), 1.99 (1H, d, $J = 4.7$ Hz, 7-OH), 1.92 (1H, ddd, $J = 14.1, 6.3, 6.3$ Hz, H-11b), 1.82 (1H, m, H-8), 1.67 (3H, s, H-26), 1.51 (1H, m, H-10_a), 1.40 (1H, m, H-9_b), 1.33 (1H, m, H-10_b), 1.31 (3H, s, H-23), 1.27 (1H, m, H-10_a), 1.23 (1H, m, H-9_a), 1.16 (3H, d, $J = 7.0$ Hz, H-24), 1.10 (1H, m, H-9_b), 1.07 (3H, s, H-22), 0.95 (3H, d, $J = 7.0$ Hz, H-25_a), 0.92 (3H, d, $J = 6.5$ Hz, H-25_b), 0.75 (1H, m, H-10_b); EIMS m/z 533 [M]⁺ XXX; HREIMS m/z 533.XXX (calcd. for C₃₀H₄₇NO₅S, 533.XXX).

Epothilone I₄ (33): colorless amorphous solid; $[\alpha]_D^{22}$ -XXX (c. XXX, MeOH); UV (MeOH) λ_{max} nm (ϵ) XXX; IR (KBr) ν_{max} XXX cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 6.95 (1H, s, H-19), 6.53 (1H, bs, H-17), 5.47 (1H, dt, $J = 11.1, 5.8$ Hz, H-12), 5.33 (1H, ddd, $J = 9.2, 3.9, 0.5$ Hz, H-15), 5.33 (1H, m, H-13), 4.09 (1H, dddd, $J = 9.6, 8.1, 4.5, 3.3$ Hz, H-3), 3.83 (1H, m, H-7), 3.57 (1H, bs, 3-OH), 2.89 (1H, dq, $J = 7.4, 7.1$ Hz, H-6), 2.83 (1H, dq, $J = 8.1, 7.1$ Hz, H-4), 2.70 (3H, s, H-21), 2.64 (1H, m, H-14a), 2.42 (1H, dd, $J = 14.2, 3.3$ Hz, H-2a), 2.43 (1H, dd, $J = 14.2, 9.6$ Hz, H-2b), 2.30 (1H, m, H-14b), 2.10 (3H, d, $J = 1.3$ Hz, H-27), 2.09 (2H, m, H-11), 1.81 (1H, m, H-8), 1.74 (1H, bd, $J = 5.6$ Hz, 7-OH), 1.53 (1H, m, H-10_a), 1.49 (1H, m, H-9_b), 1.47 (1H, m, H-10_a), 1.27 (1H, m, H-10_b), 1.24 (1H, m, H-9_a), 1.17 (3H, d, $J = 7.1$ Hz, H-23), 1.14 (1H, m, H-9_b), 1.08 (3H, d, $J = 7.1$ Hz, H-24), 0.97 (3H, d, $J = 6.9$ Hz, H-25_a),

0.91 (3H, d, $J = 6.5$ Hz, H-25_p), 0.79 (1H, m, H-10_ab); ^{13}C NMR (CDCl_3 , 100 MHz) δ 217.0 (s, C-5), 170.8 (s, C-1), 164.8 (s, C-20), 152.4 (s, C-18), 137.1 (s, C-16), 134.6 (d, C-12), 124.7 (d, C-13), 120.2 (d, C-17), 116.4 (d, C-19), 78.7 (d, C-15), 76.4 (d, C-7), 71.3 (d, C-3), 50.7 (d, C-4), 50.1 (d, C-6), 40.7 (t, C-2), 38.5 (t, C-9_w), 35.5 (t, C-10_w), 33.4 (d, C-8), 31.8 (t, C-14), 30.0 (d, C-9_p), 27.2 (t, C-11), 26.7 (t, C-10_p), 21.4 (q, C-25_p), 19.3 (q, C-21), 18.2 (q, C-25_w), 15.4 (q, C-27), 14.4 (q, C-24), 13.1 (q, C-23); EIMS m/z 505 $[\text{M}]^+$ XXX; HREIMS m/z 505.XXX (calcd. for $\text{C}_{28}\text{H}_{43}\text{NO}_5\text{S}$, 505.XXX).

Epothilone I₅ (34): colorless amorphous solid; $[\alpha]_D^{22}$ -XXX (c XXX, MeOH); UV (MeOH) λ_{max} nm (ϵ) XXX; IR (KBr) ν_{max} XXX cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.97 (1H, s, H-19), 6.52 (1H, bs, H-17), 5.32 (1H, dd, $J = 7.1, 6.2$ Hz, H-15), 5.03 (1H, dd, $J = 8.4, 5.0$ Hz, H-13), 4.05 (1H, dddd, $J = 7.5, 7.2, 5.9, 4.6$ Hz, H-3), 3.91 (1H, m, H-7), 3.17 (1H, d, $J = 5.9$ Hz, 3-OH), 2.94 (1H, dq, $J = 7.2, 7.1$ Hz, H-4), 2.87 (1H, dq, $J = 6.5, 6.9$ Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dd, $J = 14.6, 4.6$ Hz, H-2a), 2.60 (1H, m, H-14a), 2.53 (1H, dd, $J = 14.6, 7.5$ Hz, H-2b), 2.31 (1H, m, H-14b), 2.10 (3H, d, $J = 1.1$ Hz, H-27), 2.10 (1H, m, H-11a), 2.02 (1H, m, H-11b), 1.97 (1H, bd, $J = 5.6$ Hz, 7-OH), 1.84 (1H, m, H-8), 1.66 (3H, s, H-26), 1.55 (1H, m, H-9_p), 1.49 (1H, m, H-10_pa), 1.39 (1H, m, H-10_pb), 1.33 (1H, m, H-10_aa), 1.31 (1H, m, H-9_aa), 1.15 (3H, d, $J = 7.1$ Hz, H-23), 1.12 (1H, m, H-9_ab), 1.11 (3H, d, $J = 6.9$ Hz, H-24), 0.97 (3H, d, $J = 6.9$ Hz, H-25_w), 0.94 (1H, m, H-10_ab), 0.93 (3H, d, $J = 6.6$ Hz, H-25_p); EIMS m/z 519 $[\text{M}]^+$ XXX; HREIMS m/z 519.XXX (calcd. for $\text{C}_{29}\text{H}_{45}\text{NO}_5\text{S}$, 519.XXX).

Epothilone I₆ (35): colorless amorphous solid; $[\alpha]_D^{22}$ -XXX (c XXX, MeOH); UV (MeOH) λ_{max} nm (ϵ) XXX; IR (KBr) ν_{max} XXX cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.97 (1H,

s, H-19), 6.52 (1H, bs, H-17), 5.24 (1H, dd, $J = 6.9, 6.9$ Hz, H-15), 5.02 (1H, dd, $J = 8.8, 5.2$ Hz, H-13), 4.22 (1H, tdd, $J = 6.1, 5.6, 4.8$ Hz, H-3), 3.76 (1H, ddd, $J = 6.1, 5.7, 5.6$ Hz, H-7), 3.13 (1H, d, $J = 5.6$ Hz, 3-OH), 3.05 (1H, dq, $J = 4.8, 7.0$ Hz, H-4), 2.79 (1H, dq, $J = 5.6, 6.9$ Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, m, H-14a), 2.57 (2H, d, $J = 6.1$ Hz, H-2a), 2.30 (1H, m, H-14b), 2.08 (3H, d, $J = 1.0$ Hz, H-27), 2.02 (2H, m, H-11), 1.73 (1H, d, $J = 6.1$ Hz, 7-OH), 1.69 (1H, m, H-8), 1.66 (3H, s, H-26), XXX (H-9_a, H-9_b, H-10_a, H-10_b), 1.21 (3H, d, $J = 7.0$ Hz, H-22), 1.16 (3H, d, $J = 6.9$ Hz, H-24), 0.94 (3H, d, $J = 6.9$ Hz, H-25_a), 0.91 (3H, d, $J = 6.4$ Hz, H-25_b); EIMS m/z 519 [M]⁺ XXX; HREIMS m/z 519.XXX (calcd. for C₂₉H₄₅NO₅S, 519.XXX).

Epothilone K (36): colorless amorphous solid; $[\alpha]_D^{22} -7$ (c 0.08, MeOH); UV (MeOH) λ_{\max} nm (ϵ) 212 (16700), 248 (12500); IR (KBr) ν_{\max} 3431, 2963, 2927, 2856, 1731, 1712, 1262, 1093, 1021, 802 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 6.95 (1H, s, H-19), 6.51 (1H, bs, H-17), 5.49 (3H, m, H-15, H-13, and H-12), 4.04 (1H, dddd, $J = 7.9, 7.6, 6.9, 3.3$ Hz, H-3), 3.36 (1H, dq, $J = 6.9, 6.8$ Hz, H-6), 2.83 (1H, d, $J = 7.6$ Hz, 3-OH), 2.75 (1H, ddd, $J = 16.1, 6.6, 3.4$ Hz, H-14a), 2.74 (1H, dd, $J = 15.3, 3.3$ Hz, H-2a), 2.71 (3H, s, H-21), 2.58 (2H, m, H-14b and H-8), 2.50 (1H, dd, $J = 15.3, 7.9$ Hz, H-2b), 2.29 (1H, m, H-11a), 2.10 (1H, m, H-11b), 2.09 (3H, d, $J = 0.7$ Hz, H-27), 1.78 (1H, m, H-9a), 1.65 (1H, m, H-10a), 1.48 (1H, m, H-10b), 1.18 (1H, m, H-9b), 1.15 (3H, d, $J = 6.8$ Hz, H-22), 1.03 (3H, d, $J = 6.5$ Hz, H-25); EIMS m/z 405 [M]⁺ (38), 317 (12), 260 (9), 232 (10), 204 (14), 190 (16), 168 (100), 164 (30), 151 (28); HREIMS m/z 405.XXX (calcd. for C₂₆H₃₉NO₅S, 405.XXX).

(37): colorless amorphous solid; $[\alpha]_D^{22} -27.5$ (c 0.4, MeOH); UV (MeOH) λ_{\max} nm (ϵ).

211 (16100), 247 (12100); IR (KBr) ν_{\max} 3431, 2967, 2929, 2875, 1704, 1462, 1381, 1010 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.94 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.56 (1H, dtt, $J = 10.8$, 7.3, 1.4 Hz, H-12), 5.39 (1H, dtt, $J = 10.8$, 7.3, 1.4 Hz, H-13), 4.17 (1H, t, $J = 6.6$ Hz, H-15), 3.50 (1H, ddd, $J = 8.7$, 2.6, 2.6 Hz, H-7), 3.10 (1H, d, $J = 2.6$, 7-OH), 2.90 (1H, dq, $J = 2.6$, 7.2 Hz, H-6), 2.77 (1H, sep, $J = 6.9$ Hz, H-4), 2.70 (3H, s, H-21), 2.40 (2H, m, H-14), 2.07 (2H, m, H-11), 2.04 (3H, d, $J = 1.1$ Hz, H-27), 1.78 (1H, bs, 15-OH), 1.74 (1H, m, H-9a), 1.50 (1H, m, H-8), 1.46 (1H, m, H-10a), 1.27 (1H, m, H-10b), 1.11 (1H, m, H-9b), 1.094 (3H, d, $J = 6.9$ Hz, H-23), 1.089 (3H, d, $J = 6.9$ Hz, H-22), 1.08 (3H, d, $J = 7.2$ Hz, H-24), 0.82 (3H, d, $J = 6.7$ Hz, H-25); ^{13}C NMR (CDCl_3 , 100 MHz) δ 220.5 (s, C-5), 164.6 (s, C-20), 152.9 (s, C-18), 141.5 (s, C-16), 133.4 (d, C-12), 125.0 (d, C-13), 119.2 (d, C-17), 115.6 (d, C-19), 77.2 (d, C-15), 74.9 (d, C-7), 44.9 (d, C-6), 40.0 (d, C-4), 35.5 (d, C-8), 33.5 (t, C-14), 32.3 (t, C-9), 27.9 (t, C-11), 26.9 (t, C-10), 19.2 (q, C-21), 18.6 (q, C-23), 18.1 (q, C-22), 15.6 (q, C-25), 14.4 (q, C-27), 9.3 (q, C-24); EIMS m/z 407 $[\text{M}]^+$ (0.1), 204 (0.8), 168 (100), 140 (3.4); HREIMS m/z 407.XXX (calcd. for $\text{C}_{23}\text{H}_{37}\text{NO}_5\text{S}$, 407.XXX).

(38): colorless amorphous solid; $[\alpha]_D^{25} +25.0$ (c 0.5, MeOH); UV (MeOH) λ_{\max} nm (ϵ) 212 (17700), 247 (13400); IR (KBr) ν_{\max} 3427, 2971, 2933, 2878, 2858, 1709, 1457, 1377, 1186, 1023 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.95 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.52 (1H, dtt, $J = 10.9$, 7.2, 1.4 Hz, H-12), 5.39 (1H, dtt, $J = 10.9$, 7.1, 1.2 Hz, H-13), 4.18 (1H, ddt, $J = 3.4$, 0.4, 6.7 Hz, H-15), 2.71 (3H, s, H-21), 2.51 (1H, bq, $J = 6.8$ Hz, H-8), 2.48 (1H, dq, $J = 17.7$, 7.4 Hz, H-6a), 2.41 (1H, dq, $J = 17.7$, 7.2 Hz, H-6b), 2.39 (2H, ddd, $J = 7.1$, 6.7, 1.4 Hz, H-14), 2.06 (2H, ddt, 7.2, 1.2, 7.0 Hz, H-11), 2.05 (3H, d, $J = 1.4$ Hz, H-27), 1.81 (1H, d, $J = 3.4$ Hz,

15-OH), 1.66 (1H, m, H-9a), 1.32 (1H, m, H-9b), 1.31 (2H, m, H-10), 1.06 (3H, d, $J = 6.9$ Hz, H-25), 1.04 (3H, dd, $J = 7.4, 7.2$ Hz, H-24); ^{13}C NMR (CDCl_3 , 75 MHz) δ 215.3 (s, C-7), 164.6 (s, C-20), 152.9 (s, C-18), 141.5 (s, C-16), 132.7 (d, C-12), 125.3 (d, C-13), 119.2 (d, C-17), 115.6 (d, C-19), 77.2 (d, C-15), 46.0 (d, C-8), 34.3 (t, C-14), 33.5 (t, C-6), 32.7 (t, C-9), 27.5 (t, C-11), 27.3 (t, C-10), 19.2 (q, C-21), 16.5 (q, C-25), 14.4 (q, C-27), 7.8 (q, C-24); EIMS m/z 335 [M] $^+$ (2), 317 (4), 170 (27), 169 (67), 168 (100), 140 (20); HREIMS m/z 335.1912 (calcd. for $\text{C}_{19}\text{H}_{29}\text{NO}_2\text{S}$, 335.1919).

(39): colorless amorphous solid; $[\alpha]_D^{22} +26.4$ (c 0.27, MeOH); UV (MeOH) λ_{max} nm (ϵ) 203 (19100), 244 (12500); IR (KBr) ν_{max} 3430, 2970, 2934, 2877, 1710, 1458, 1377, 1184 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.94 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.17 (1H, t, $J = 7.3$ Hz, H-13), 4.13 (1H, m, H-15), 2.70 (3H, s, H-21), 2.51 (1H, bq, $J = 6.8$ Hz, H-8), 2.47 (1H, dq, $J = 17.7, 7.2$ Hz, H-6a), 2.41 (1H, dq, $J = 17.7, 7.2$ Hz, H-6b), 2.33 (2H, bdd, $J = 7.3, 6.8$ Hz, H-14), 2.05 (3H, d, $J = 1.2$ Hz, H-27), 2.03 (2H, m, H-11), 1.71 (1H, d, $J = 3.2$ Hz, 15-OH), 1.69 (3H, d, $J = 1.3$ Hz, H-26), 1.62 (1H, m, H-9a), 1.32 (3H, m, H-10 and H-9b), 1.06 (3H, d, $J = 6.9$ Hz, H-25), 1.03 (3H, t, $J = 7.2$ Hz, H-24); EIMS m/z 349 [M] $^+$ (0.7), 331 (1.7), 168 (100), 140 (5.1); HREIMS m/z 349.XXX (calcd. for $\text{C}_{20}\text{H}_{31}\text{NO}_2\text{S}$, 349.XXX).

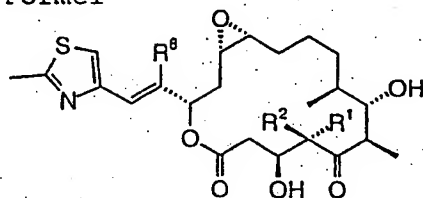
Tab 1. Aktivität von Epothilonen und Verbindungen (1) bis (39) gegen Maus-Fibroblasten (L929, IC50 /ng/ml/)

Struktur- typ	Epothilone				
	A _r	B _r	C _r	D _r	trans C _r
Ausgangs- epothilon	(1) 4	(2) 1-2	(14) 50-100	(15) 20	-
21-Hydroxy (E&F)	(3) 10	(4) 1.5	-	-	-
Oxazoles (G&H)	(10) 6	(11) 1	(12) 120	(13) 11	-
(R)-4-Desmethyl (X ₁)	(5) 20	-	(16) 200	(17) 20	(28) 400
(S)-4-Desmethyl (X ₂)	(6) 7	-	(18) 25-30	(19) 12	(29) 80
6-Desmethyl (X ₃)	-	-	(20) 1500	-	-
8-Desmethyl (X ₄)	-	-	(21) 800	-	-
8,9-Dehydro (X ₅)	-	-	(22) 1500	(23) 200	-
10,11-Dehydro (X ₆)	-	-	(24) 120	-	-
14-Hydroxy (X ₇)	-	-	(25)	-	-
16-Desmethyl (X ₈)	(7) 20	-	(26) 250	-	-
27-Hydroxy (X ₉)	(8) 100	-	(27) 200	-	-
21-Methyl (X ₁₀)	-	(9) 1.5	-	-	-
Verbindung	-	-	(36) 180	-	-
Verbindung	-	-	(37) 50	-	-
Verbindung	-	-	(38) 2000	(39) 500	-

Epothilon-Nebenkomponenten

Patentansprüche

1. Epothilon der Formel



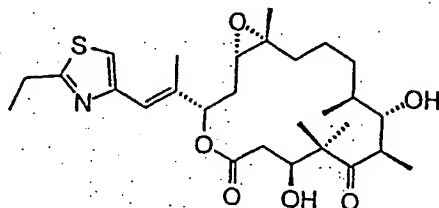
Epothilone A₁ (5) R¹ = H; R², R⁸ = Me

Epothilone A₂ (6) R² = H; R¹, R⁸ = Me

Epothilone A₈ (7) R⁸ = H; R¹, R² = Me oder

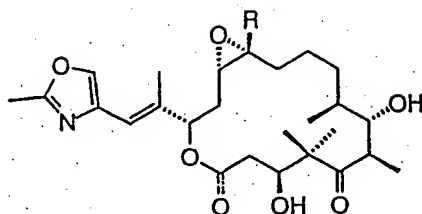
Epothilone A₉ (8) R¹ = CH₂OH; R², R⁸ = Me

2. Epothilon der Formel



Epothilone B₁₀ (9)

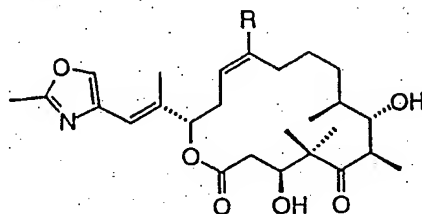
3. Epothilon der Formel

✓ Epothilone G₁ (10) R = H

oder

✓ Epothilone G₂ (11) R = Me

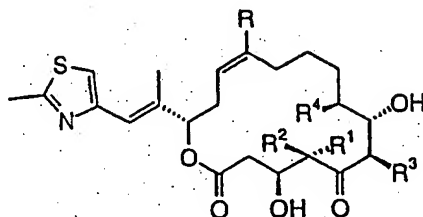
4. Epothilon der Formel

✓ Epothilone H₁ (12) R = H

oder

✓ Epothilone H₂ (13) R = Me

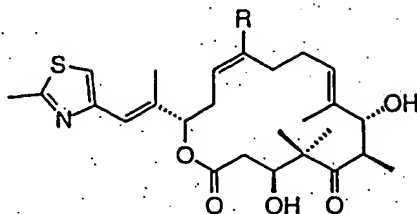
5. Epothilon der Formel

✓ Epothilone C₁ (16) R¹ = H; R², R³, R⁴ = Me; R = H✓ Epothilone D₁ (17) R¹ = H; R², R³, R⁴ = Me; R = Me✓ Epothilone C₂ (18) R² = H; R¹, R³, R⁴ = Me; R = H✓ Epothilone D₂ (19) R² = H; R¹, R³, R⁴ = Me; R = Me✓ Epothilone C₃ (20) R³ = H; R¹, R², R⁴ = Me; R = H

oder

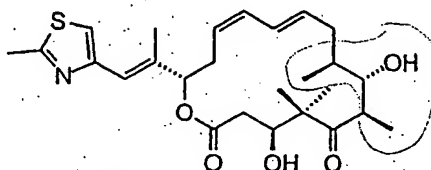
✓ Epothilone C₄ (21) R⁴ = H; R¹, R², R³ = Me; R = H

6. Epothilon der Formel

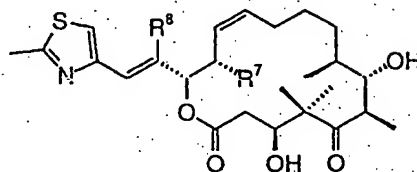
Epothilone C₅ (22) R = HEpothilone D₅ (23) R = Me

oder

7. Epothilon der Formel

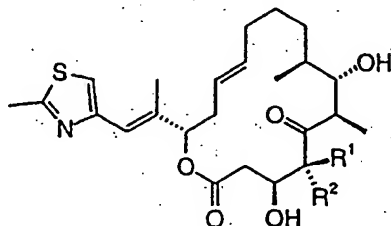
✓ Epothilone C₆ (24)

8. Epothilin der Formel

✓ Epothilone C₇ (25) R⁷ = OH; R⁸ = Me✓ Epothilone C₈ (26) R⁸, R⁷ = H✓ Epothilone C₉ (27) R⁸ = CH₂OH; R⁷ = H

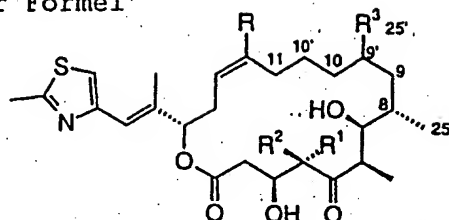
oder

9. Epothilon der Formel

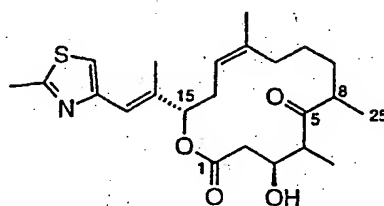
✓ trans-Epothilone C₁ (28) R¹ = H; R² = Me✓ trans-Epothilone C₂ (29) R² = H; R¹ = Me

oder

10. Epothilon der Formel

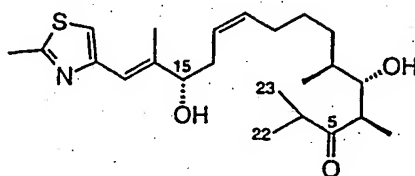
Epothilone I₁ (30) R, R³ = H; R¹, R² = MeEpothilone I₂ (31) R = H; R¹, R², R³ = MeEpothilone I₃ (32) R¹, R², R³, R = MeEpothilone I₄ (33) R², R = H; R¹, R³ = MeEpothilone I₅ (34) R² = H; R¹, R³, R = Me oderEpothilone I₆ (35) R¹ = H; R², R³, R = Me

11. Epothilon der Formel



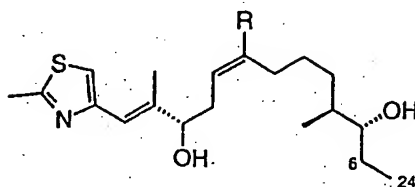
✓ Epothilone K (36)

12. Verbindung der Formel



(37)

13. Verbindung der Formel



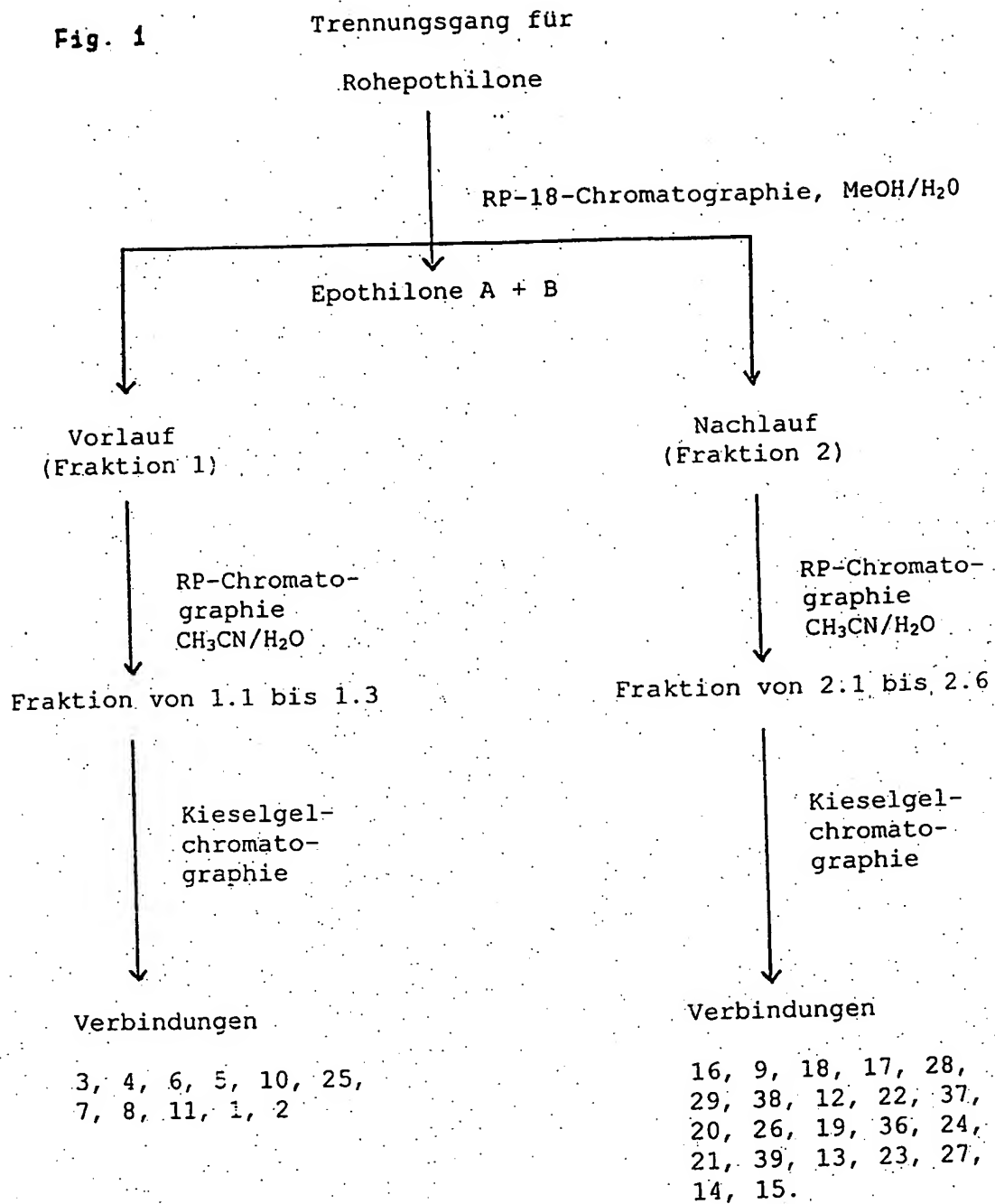
(38) R = H

(39) R = Me
32

oder

1/2

Fig. 1



2/2

Fig. 2

fraction 1	1.1	Epothilone E (3)	variable ^a
		Epothilone F (4)	variable ^a
		Epothilone A ₂ (6)	14.5 mg
		Epothilone A ₁ (5)	3.1 mg
		Epothilone G ₁ (10)	62.3 mg
	1.2	Epothilone C ₇ (25)	0.9 mg
		Epothilone A ₃ (7)	38.7 mg
	1.3	Epothilone A ₄ (8)	4.4 mg
		Epothilone G ₂ (11)	9.4 mg
fraction 2	2.1	Epothilone A (1)	29800.0 mg
		Epothilone B (2)	10300.0 mg
		Epothilone C ₁ (16)	32.4 mg
	2.2	Epothilone B ₁₀ (9)	1.1 mg
		Epothilone C ₂ (18)	58.4 mg
	2.3	Epothilone D ₁ (17)	5.3 mg
		trans-Epothilone C ₁ (28)	1.4 mg
		trans-Epothilone C ₂ (29)	4.5 mg
		38	6.5 mg
		Epothilone H ₁ (12)	3.0 mg
		Epothilone C ₃ (22)	7.3 mg
	2.4	37	2.9 mg
		Epothilone C ₃ (20)	32.5 mg
		Epothilone C ₄ (26)	26.3 mg
		Epothilone D ₂ (19)	13.1 mg
		Epothilone K (36)	0.4 mg
	2.5	Epothilone C ₅ (24)	2.9 mg
		Epothilone C ₄ (21)	6.5 mg
		39	0.8 mg
	2.6	Epothilone H ₂ (13)	1.5 mg
		Epothilone D ₃ (23)	0.9 mg
		Epothilone C ₅ (27)	3.0 mg
		Epothilone C (14)	4600.0 mg
		Epothilone D (15)	2700.0 mg

PCT

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INTERNATIONALE ANMELDUNG VERÖFFENTLICHT NACH DEM VERTRAG ÜBER DIE
INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT)

(51) Internationale Patentklassifikation ⁶ : C07D 493/04, 417/06, 413/06, 277/24 // (C07D 493/04, 313:00, 303:00)		A3	(11) Internationale Veröffentlichungsnummer: WO 99/65913
		(43) Internationales Veröffentlichungsdatum:	23. Dezember 1999 (23.12.99)
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(22) Internationales Anmeldedatum: 18. Juni 1999 (18.06.99)		Veröffentlicht <i>Mit internationalem Recherchenbericht.</i> <i>Vor Ablauf der für Änderungen der Ansprüche zugelassenen Frist. Veröffentlichung wird wiederholt falls Änderungen eintreffen.</i>	
(30) Prioritätsdaten: 198 26 988.9 18. Juni 1998 (18.06.98) DE			
(71) Anmelder (für alle Bestimmungsstaaten ausser US): GESELLSCHAFT FÜR BIOTECHNOLOGISCHE FORSCHUNG MBH (GBF) [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE).		(88) Veröffentlichungsdatum des internationalen Recherchenberichts: 20. April 2000 (20.04.00)	
(72) Erfinder; und (75) Erfinder/Anmelder (nur für US): HOEFLE, Gerhard [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). REICHENBACH, Hans [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). GERTH, Klaus [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). HARDT, Ingo [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). SASSE, Florenz [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). STEINMETZ, Heinrich [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE).			
(74) Anwälte: BOETERS, Hans usw.; Boeters & Bauer, Bereiteranger 15, D-81541 München (DE).			
(54) Title: EPOTHILONE MINOR CONSTITUENTS			
(54) Bezeichnung: EPOTHILON-NEBENKOMPONENTEN			
(57) Abstract <p>The invention relates to compounds which are obtained by fermenting DSM 6773, especially epothilones A1, A2, A8; A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 and K and trans-epothilones C1 and C2.</p>			
(57) Zusammenfassung <p>Die Erfindung betrifft Verbindungen, die durch Fermentation von DSM 6773 erhältlich sind, insbesondere Epothilone A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 und K und Trans-Epothilone C1 und C2.</p>			

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Codes zur Identifizierung von PCT-Vertragsstaaten auf den Kopfbögen der Schriften, die internationale Anmeldungen gemäss dem PCT veröffentlichen.

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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 99/04244

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07D493/04 C07D417/06 C07D413/06 C07D277/24
 //(C07D493/04.313:00.303:00)

According to International Patent Classification (IPC) or to both national classification and IPC

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Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 08849 A (NOVARTIS AKTIENGESELLSCHAFT ;BAUER ARMIN (DE); CORDES MARTIN (DE);) 5 March 1998 (1998-03-05) abstract; claims; examples	1-13
X	WO 98 22461 A (BIOTECHNOLOG FORSCHUNG GMBH ;GERTH KLAUS (DE); HOEFLE GERHARD (DE)) 28 May 1998 (1998-05-28) abstract; claims; examples	1-13
X	WO 97 19086 A (BIOTECHNOLOG FORSCHUNG GMBH ;KIFFE MICHAEL (DE); HOEFLE GERHARD (D) 29 May 1997 (1997-05-29) abstract; claims; examples	1-13

☒ Further documents are listed in the continuation of box C.

X Patent family members are listed in annex.

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Date of the actual completion of the international search

22 February 2000

Date of mailing of the International search report

07/03/2000

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 99/04244

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NICOLAOU K C ET AL: "DESIGNED EPOTHILONES: COMBINATORIAL SYNTHESIS, TUBULIN ASSEMBLY PROPERTIES, AND CYTOTOXIC ACTION AGAINST TAXOL-RESISTANT TUMOR CELLS" ANGEWANDTE CHEMIE. INTERNATIONAL EDITION, DE, VERLAG CHEMIE. WEINHEIM, vol. 36, no. 19, 1 January 1997 (1997-01-01), pages 2097-2103, XP002064441 ISSN: 0570-0833 page 2099 -page 2100	1-13
X	NICOLAOU ET AL: "Total synthesis of oxazole- and cyclopropane-containing epothilone A analogs by the olefin metathesis approach" CHEMISTRY - A EUROPEAN JOURNAL, US, VCH PUBLISHERS, vol. 3, no. 12, 1997, pages 1957-1970, XP002121565 ISSN: 0947-6539 page 1959 -page 1961	1-13
X	BALOG A ET AL: "Stereoselective Syntheses and Evaluation of Compounds in the 8-Desmethylepothilone A Series: Some Surprising Observations Regarding Their Chemical and Biological Properties" TETRAHEDRON LETTERS, NL, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, vol. 38, no. 26, 30 June 1997 (1997-06-30), pages 4529-4532, XP004074826 ISSN: 0040-4039 the whole document	1-13
X	SU D -S ET AL: "STRUCTURE - ACTIVITY RELATIONSHIPS OF THE EPOTHILONES AND THE FIRST IN VIVO COMPARISON WITH PACLITAXEL" ANGEWANDTE CHEMIE. INTERNATIONAL EDITION, DE, VERLAG CHEMIE. WEINHEIM, vol. 36, no. 19, 1997, pages 2093-2096, XP002916075 ISSN: 0570-0833 page 2094 -page 2095	1-13
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Information on patent family members

International application No
PCT/EP 99/04244

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
W0 9808849 A	05-03-1998	DE 19636343 C	23-10-1997
		DE 19645361 A	30-04-1998
		DE 19645362 A	30-04-1998
		AU 2149397 A	19-03-1998
		EP 0923583 A	23-06-1999
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		EP 0873341 A	28-10-1998
		EP 0903348 A	24-03-1999

INTERNATIONALER RECHERCHENBERICHT

International . Alterszeichen

PCT/EP 99/04244

A. KLASSIFIZIERUNG DES ANMELDUNGSGEGENSTANDES

IPK 6 C07D493/04 C07D417/06 C07D413/06 C07D277/24
 //(C07D493/04,313:00,303:00)

Nach der internationalen Patentklassifikation (IPK) oder nach der nationalen Klassifikation und der IPK

B. RECHERCHIERTE GEBIETE

Recherchiertes Mindestprüfstoff (Klassifikationssystem und Klassifikationssymbole)

IPK 6 C07D

Recherchierte aber nicht zum Mindestprüfstoff gehörende Veröffentlichungen, soweit diese unter die recherchierten Gebiete fallen

Während der internationalen Recherche konsultierte elektronische Datenbank (Name der Datenbank und evtl. verwendete Suchbegriffe)

C. ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
X	WO 98 08849 A (NOVARTIS AKTIENGESELLSCHAFT ;BAUER ARMIN (DE); CORDES MARTIN (DE);) 5. März 1998 (1998-03-05) Zusammenfassung; Ansprüche; Beispiele	1-13
X	WO 98 22461 A (BIOTECHNOLOG FORSCHUNG GMBH ;GERTH KLAUS (DE); HOEFLE GERHARD (DE)) 28. Mai 1998 (1998-05-28) Zusammenfassung; Ansprüche; Beispiele	1-13
X	WO 97 19086 A (BIOTECHNOLOG FORSCHUNG GMBH ;KIFFE MICHAEL (DE); HOEFLE GERHARD (D) 29. Mai 1997 (1997-05-29) Zusammenfassung; Ansprüche; Beispiele	1-13
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☒ Weitere Veröffentlichungen sind der Fortsetzung von Feld C zu entnehmen

Y Siehe Anhang Patentfamilie

* Besondere Kategorien von angegebenen Veröffentlichungen :

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Datum des Abschlusses der internationalen Recherche

22. Februar 2000

Abgabedatum des internationalen Rechercheberichts

07/03/2000

Name und Postanschrift der internationalen Recherchenbehörde
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Bevollmächtigter Bediensteter

Paisdor, B

INTERNATIONALER RECHERCHENBERICHT

International / Aktenzeichen
PCT/EP 99/04244

C.(Fortsetzung) ALS WESENTLICH ANGESEHENE UNTERLAGEN		
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X	<p>NICOLAOU ET AL: "Total synthesis of oxazole- and cyclopropane-containing epothilone A analogs by the olefin metathesis approach"</p> <p>CHEMISTRY - A EUROPEAN JOURNAL,US,VCH PUBLISHERS, Bd. 3, Nr. 12, 1997, Seiten 1957-1970, XP002121565 ISSN: 0947-6539 Seite 1959 -Seite 1961</p>	1-13
X	<p>BALOG A ET AL: "Stereoselective Syntheses and Evaluation of Compounds in the 8-Desmethylepothilone A Series: Some Surprising Observations Regarding Their Chemical and Biological Properties"</p> <p>TETRAHEDRON LETTERS,NL,ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, Bd. 38, Nr. 26, 30. Juni 1997 (1997-06-30), Seiten 4529-4532, XP004074826 ISSN: 0040-4039 das ganze Dokument</p>	1-13
X	<p>SU D -S ET AL: "STRUCTURE - ACTIVITY RELATIONSHIPS OF THE EPOTHILONES AND THE FIRST IN VIVO COMPARISON WITH PACLITAXEL"</p> <p>ANGEWANDTE CHEMIE. INTERNATIONAL EDITION,DE,VERLAG CHEMIE. WEINHEIM, Bd. 36, Nr. 19, 1997, Seiten 2093-2096, XP002916075 ISSN: 0570-0833 Seite 2094 -Seite 2095</p>	1-13

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International Aktenzeichen
PCT/EP 99/04244

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Angaben zu Veröffentlichungen, die zur selben Patentfamilie gehören

Internationales Aktenzeichen
PCT/EP 99/04244

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